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Mucous Colitis*

Observations in 500 Cases,

By Julius Friedenwald, M.D., Maurice Feldman, M.D., and Lewis J. Rosenthal, M.D., *Baltimore, Maryland*

MUCOUS COLITIS may be characterized as an affection in which more or less mucus is discharged from the bowel usually associated with colic and in which functional nervous manifestations are prominent.

The first allusion to colitis is noted in Chronicles II, Chapter 21, verses 12-19. "Thou shalt have great sickness by disease of thy bowels until thy bowels fall out by reason of the sickness day by day." It was first accurately described by Richard Powell in 1818 and in this country by Mason Good[2] (1825) under the name of diarrhea tubularis. According to Woodward, however, Fernelius[3] was the first to draw attention to this condition.

In modern times, the first accurate accounts of this affection were given by DaCosta[4] in this country and by Von Leyden[5] in Germany which were further followed by an important description by Nothnagel[6] who suggested the term "mucous colic."

Etiology. Three views as to the nature of this condition have been maintained.

1. That it is purely neurogenic and that the mucus produced is entirely a nervous hypersecretion a conclusion recently again emphasized by Bockus, Bank and Wilkinson.[7]

2. That it is catarrhal in nature produced as the result of inflammation of the mucus membrane of the colon.

3. That it is in part neurogenic and in part inflammatory.

Although there has been much discussion authorities have not agreed definitely regarding the etiology of this affection. In a few instances in which autopsy findings have been recorded definite catarrh with increased production of mucus forming cells have been observed while in others no abnormality was discovered. Hurst[8] concludes that the constant appearance of epithelial cells in various stages of degeneration with the addition of leucocytes which are frequently noted in mucous colitis is evidence sufficient to indicate the presence of a definite inflammatory affection.

Certain authorities as Nothnagel[6] in order to harmonize these conflicting views contend that there may be two varieties of this condition: one a mucous colitis of nervous origin and the other of inflammatory nature. However, as Hurst[8] points out these are probably varieties of the same condition bearing somewhat the same rela-

*From the Gastro-Enterological Clinic of the Department of Medicine of the University of Maryland.

†Presented by title at the Meeting of the Association of American Physicians at Atlantic City, May, 1929.

tion as is observed in asthma as compared with bronchitis.

From a study of our cases together with a rather careful review of the extensive literature of this subject, we feel justified in drawing the conclusion, that mucous colitis is purely of neurogenic origin and that the discharged mucus can be considered entirely in the light of a nervous hypersecretion. This stage may continue on with exacerbations and remissions for a considerable period of time associated with spasticity of the colon from which recovery may occur, or in some instances, due to a lowered resistance of the bowel, infection may take place with the production of inflammatory changes of a more or less intense type which may finally eventuate in the production of an ulcerative colitis. A number of instances in which these changes have occurred have been observed by us. Attention must also be directed to the fact that the inflammatory process may be localized high in the bowel and, therefore, cannot be visualized by proctoscopic examination. In this connection it is important to bear in mind, that moderate amounts of mucus are secreted normally by the bowel, which have no actual significance and in fact are protective and serve to inhibit the production of pathological changes.

In considering the etiology of mucous colitis the neurogenic factor must always be taken into consideration; first, inquiry into the causes and mode of development primarily reveals the fact that this condition usually occurs in nervous individuals. The patients almost invariably reveal signs of functional nervous disturbance. The changes in the nervous system have usually existed prior to the development of the intestinal affection. Bockus, Bank and Wilkinson[7] conclude that the etiology of mucous colitis is closely associated with alteration of function of the vegetative nervous system.

While there can be no question, therefore, that there are a number of factors entering into the etiology of mucous colitis, this condition manifests itself mainly in individuals prepared by an instability of the nervous system. The vegetative nervous system supplies two sets of nerve fibres to the gastro-intestinal tract, the one functioning as activator and the other as inhibitor nerves, the two combined exhibiting a regulating mechanism controlling the interactivity of both groups. In the first set we have the parasympathetic system, the stimulation of which results in the production of increased secretory and motor activity of the bowel leading to excessive formation of mucus and to colic. In the second set we have the inhibitory fibres as found in the sympathetic system stimulation of which inhibits secretion and motor activity. The action of the two systems is antagonistic; however under normal conditions a state of equilibrium exists which results in normal function of secretion and motility of the colon. When this state is interrupted, in that there be overstimulation of the parasympathetic system or inhibition of the sympathetic secretion of mucus and painful spasm may occur.

The maintenance of increased tonus of the motor fibres alone of the parasympathetic system leads to enterospasm or spastic colitis; when in ad-

Shows a string sign in a small portion of the lower bowel.

dition the secretory fibres are involved mucous colitis is produced. In the study of this disorder, it becomes evident that the instability and abnormal irritability of the nervous system is a factor of considerable importance in its etiology and most authorities contend, that the nervous element (vagotonia), as commonly observed in neurasthenics, the hysterical and hypochondriacs, plays an important rôle in this respect. However, according to Bockus[7] and his collaborators there is often evidence not only of vagotonia but also of sympathicotonia.

The constitutional factor from an etiological standpoint has not been sufficiently emphasized. There is sufficient evidence in many instances to indicate a correlation between physical type in the form of the asthenic individual and the secretory and motor disturbances noted in mucous colitis. We have here a predisposition to the production of a dysfunction in an area of least resistance, a predisposition which becomes greatly accentuated by such general factors as prolonged nervous strains and emotions.

As a basis of this study of mucous colitis we have collected 500 cases which have come under our observation. In this condition the following are recognized as contributory factors frequently associated with the development of this affection.

(1) Chronic Constipation. Chronic constipation according to Nothnagel[6] as well as Hurst[8] and Von Noorden[9] plays an important rôle as a predisposing factor, however, only in nervous individuals. The constipation is usually of the spastic type and is frequently increased by nervous upsets. Bockus on the other hand considers this condition a result rather than a cause of the mucous colitis. Constipation existed in 360 of our cases (72 per cent).

(2) Visceroptosis. Attention has already been directed to the occurrence of mucous colitis as a constitutional defect. There is little question, but that this element plays an important rôle in the etiology of mucous colitis in hypothenic individuals affected with visceroptosis. Enteroptosis occurred in 293 of our cases (58 per cent). In this series 64 per cent of the cases were of the asthenic type and 10 per cent hyperthenic.

(3) Chronic Diseases of the Gall Bladder and Appendix. Gall bladder affections are frequently associated with mucous colitis. At times the discomfort due to the colitis is so pronounced as to mask the symptoms produced by the gall bladder affection. Chronic appendicitis likewise gives rise to this condition. It is frequently associated with an intestinal stasis. With the removal of the gall bladder or appendix in these cases a cure of the colitis is often effected. On the other hand appendectomy has frequently been performed in cases of mucous colitis in which the diagnosis had been made as appendicitis and in which the absence of relief following operation led finally to the correct diagnosis. Chronic cholecystitis occurred in 92 of our cases (18 per cent) and chronic appendicitis in 65 cases (13 per cent).

(4) Chronic Disease of the Female Generative Organs.

Pelvic disorders especially in females, as prolapse of the uterus,

dysmenorrhea and pelvic inflammatory conditions are commonly associated with mucous colitis. The intestinal affection frequently becomes aggravated when exacerbations of the pelvic disorder occurs. Menstruation at times causes an increase in the symptoms in patients affected with mucous colitis, a condition which also occurs not infrequently at the menopause. Pelvic disease was noted in 76 of our cases (15 per cent).

(5) Endocrine disturbances. Colitis is often associated with abnormal endocrine function. Of these thyroid and suprarenal dysfunction are most frequent. Both hyper- and hypothyroid states are observed in this condition. Hyperthyroidism was noted in 29 of our cases (5 per cent) and hypothyroidism in 15 (3 per cent).

(6) Food Allergy. Vaughan[10] in 1922 first recorded a possible allergic factor in the causation of mucous colitis and Duke[11] and Andresen[12] described instances in which food allergy caused gastrointestinal colic, Holland[13] and more recently again, Vaughan[14] have reported cases of mucous colitis due to food hypersensitiveness. This condition was noted in 9 of our cases (1 per cent).

(7) Abdominal Adhesions. Pericolitis due to adhesions involving the colon is frequently a causative factor in the production of this disease. Adhesions often arise following abdominal operations and were present in 185 of our cases (37 per cent).

(8) Gastric Dyspepsia. It is not unusual to observe in patients affected with mucous colitis pronounced forms of gastric dyspepsia. As a constitutional defect gastroptosis is not uncommon, and in consequence gaseous distention, eructations following meals, pain, nausea and vomiting may occur. Tacchycardia is not uncommon. In some instances the stomach may itself present no abnormalities, and yet the gastric symptoms occur associated with meals, which may be accounted for by the well known gastro-colic reflex. Gastric symptoms were present in 321 of our cases (64 per cent).

(9) Intestinal Dyspepsia and Stasis. The dyspepsia may be either of the fermentative or putrefactive type and under either condition may finally terminate in a mucous colitis. Intestinal stasis also plays an important rôle in the etiology of this affection. The stagnation in the bowel may lead to the development of high degrees of putrefaction with infection of the mucosa, and finally be followed by a mucous colitis. In our series intestinal stasis with dyspepsia was observed in 136 instances (27 per cent). Inasmuch as intestinal stasis is so frequently associated with mucous colitis a subsequent toxemia not uncommonly results.

Occasionally as has already been pointed out in certain instances of mucous colitis of long standing severe infection may follow with the production of more or less serious types of ulcerative colitis. In these cases the stool becomes more or less diarrheic, contains mucus, blood and pus, is extremely fermented and offensive and fever may develop. It is in these instances that either bacteria of the proteolytic (colon group) or of the saccharo-butyric type are found predominant in the stool.

(10) Focal infections. Mucous co-

Shows a long string sign involving the entire lower colon.

litis may undoubtedly develop in some instances as a result of focal lesions in the teeth, tonsils, sinuses or gall bladder. There was direct evidence of focal infection in 118 of our cases (23 per cent).

It is not uncommon according to our experience that a number of the factors above noted may act together as causative agents in the production of mucous colitis.

Incidence. Mucous colitis occurs most frequently in the female sex. It has been estimated that the usual proportion of females to males affected is as five to one. The disease is most common in middle life and especially noted between the 20th and 40th years. It occurs however in old age and cases have been recorded in children. In our series of 500 cases there were 424 females and 76 males, a proportion of about 5½ females to 1 male.

The following presents these cases arranged according to age and sex:

Ages	Females	Males
10 to 20	18	5
20 to 30	101	16
30 to 40	114	19
40 to 50	88	21
50 to 60	84	10
60 to 70	19	5
Total	424 (84%)	76 (15%)

Pathology. Although there has been much discussion, there still remains a considerable difference of opinion regarding the pathological changes occurring in the bowel in mucous colitis. Opportunities of performing autopsies upon patients affected with this condition have been rare so that but little is known of the actual pathology of this affection. In certain specimens of colons removed at operation the mucosa has been found normal, but the mucous glands and follicles are usually observed distended with mucus, congested and inflammatory changes are noted. The discharge of mucus in the form of membrane frequently contains epithelial cells in large numbers in various stages of degeneration, indicating an unquestionable profuse desquamation from the mucous membrane of the bowel, and when, as Hurst[8] points out, leucocytes are also present additional evidence is afforded to indicate the inflammatory nature of the process. It is interesting to note, as Bastedo[15] has recently pointed out, and which is in accord with our experimental observations, that the disease is not limited entirely to the colon but also at times invades the lower ileum.

Norman and Eggston[16] group the intestinal toxemias occurring in advanced forms of mucous colitis into two types.

(1) Putrefactive toxemia
  (a) Indolic type with indicanuria
  (b) Indolic type without indicanuria
  (c) Butyric acid types.
(2) Pyogenic infective toxemia associated with focal infection of the bowel.

According to these observers, the pathological changes noted in intestinal stasis with mucous colitis are hyperplasia of the intestinal chain of lymphatics; diffuse infiltration of the intestinal mucosa with lymphocytes, eosinophiles, plasma cells, and in some instances areas of polymorphonuclear

infiltration forming small abscesses. In the more chronic cases, the submucosa is fibrous and reveals hyperplastic lymph follicles and diffuse infiltration of mononuclear cells. The muscular coat becomes next invaded and presents inflammatory infiltration with fibrosis and a partial destruction of smooth musculature. In consequence of the fibrosis a loss of elasticity of the wall of the bowel is produced, resulting in intermittent dilatation of the intestines and finally chronic dilatation with thinning of the colonic wall.

Microorganisms of many forms have been observed in the stools in cases of mucous colitis, but none of etiological importance has been determined.

Symptomatology. The most common symptoms are chronic constipation associated with colicky pain and the passage of mucus. Colicky pain may however be absent and is frequently replaced by simple abdominal discomfort. Many of these patients present a history of long standing and increasing constipation often dating back to childhood and not uncommonly associated with neurasthenic symptoms.

Previous to the first attack premonitory dyspeptic symptoms consisting of pressure, fulness, distention, flatulency and abdominal discomfort often occurs. At this period, the passage of small bits of mucus are not infrequently noted mainly surrounding the hard fecal masses. The first attack is usually ushered in suddenly with or without apparent cause with intense colicky pain followed by the passage of mucus. The immediate cause of the attack is often attributed to an increasing constipation, to nervous excitement, fatigue, menstrual disturbances or even errors in diet. The mucus is discharged in large amounts in a single evacuation or in small quantities at short intervals. Its passage is usually followed by relief from pain. The mucus frequently surrounds small scybala or is discharged with the feces or alone. In some instances, even of a severe type the passage of the membrane occurs without pain. This is however unusual though it occurred in a number of instances in our series. Not infrequently, however, following severe attacks of colic, mild forms are apt to occur also followed by a mucous discharge.

In the intervals between the attacks the patient is frequently in comfort, though in many instances dyspeptic symptoms with dull abdominal pain occur, not uncommonly associated with psychoneurotic manifestations and persistent lassitude. The duration of the interval between attacks is variable. In some instances a few days may elapse between attacks while in others there may be weeks, or even months.

The attack itself is ordinarily of several hours duration from the time of the onset of the colic to the final completion of the mucus discharge; though in rare instances it may extend with minor remissions over a period of days. It is frequently accompanied by nausea, vomiting, weakness and occasionally with signs of shock. Occasionally mucus is vomited at this stage, and a rise in temperature may occur. The pain is most commonly noted in the left lower abdomen and

Same case, illustrates the absence of haustra, following a colon enema.

there is usually tenderness in this region as well as along the course of the descending colon. The pain is not infrequently relieved by a movement of the bowels. Contracted painful areas can at times be palpated in the region of the descending colon and sigmoid, indicating a spasticity of the bowel. Similar manifestations are less frequently observed in the region of the cecum ascending and transverse colon, and may lead to an erroneous diagnosis of appendicitis, cholecystitis or diverticulitis.

Patients affected with mucous colitis as has already been noted usually suffer with chronic constipation of so severe a type that the most drastic remedies are often required to secure proper bowel evacuations.

According to Von Noorden[17] constipation which is of the spastic type, occurs in at least 80 per cent of the cases. At times the constipation may be followed by diarrhea which may continue for a period of days. This is produced by the irritation of the feces retained over days inducing an actual colitis which however may again disappear after a short interval or continue on to produce a definite chronic colitis. In fact, Mallory[18] maintains that ulcerative colitis is but the final stage of mucous colitis. In a small proportion of cases constipation is entirely absent, the discharges being normal in consistency or even soft. This has been estimated to occur in about 20 per cent of cases. In these cases there is present in addition to the excess of mucus in the stools, evidences of fermentation indicated by the presence of gas bubbles and an extremely fetid acid odor together with a resultant putrefactive and pyogenic infective toxemia. Occasionally blood is found in the stools in mucous colitis though this is rather rare.

Boas[19] has recently called attention to a symptom observed at times in mucous colitis which he terms pyrosis coli—a burning pain along the course of the colon, and associated with the chronic constipation and discharge of mucus. This condition is independent of the ingestion of food, and is probably due to excessive fermentation in the bowel. In our series typical attacks of mucus colic were observed in 250 instances (50 per cent); in 185 (37 per cent) there was more or less generalized abdominal pain and discomfort, and in 39 (7 per cent) pain was entirely absent although indigestion and abdominal discomfort was noted. It was more particularly localized in the lower left quadrant in 91 instances (18 per cent); in the upper abdomen in 38 (7 per cent); in the lower right quadrant in 12 (3 per cent); in the upper right quadrant in 23 (4 per cent); in the upper left quadrant in 32 (6 per cent); in the umbilical region in 38 (7 per cent) and in the lumbar region in 11 (2 per cent). In 52 (10 per cent) it was variable in location. Tenderness on pressure was noted over the entire colon in 213 instances (42 per cent); it was almost entirely limited to the lower descending colon in 96 (13 per cent) to the ascending colon in 28 (5 per cent) and to the transverse colon in 9 (1 per cent).

Chronic constipation existed in 360 of our cases (72 per cent); alternating constipation and diarrhea occurred in 54 (10 per cent); diarrhea in 45 in-

stances (9 per cent); normal bowel movements were noted in 10 instances (2 per cent).

The Mucus. The glands of the colon secrete the mucus which is converted into shreds, compact masses and membranes and at times soft gelatinous material. The appearance often indicates that the passage of these membranes is not immediate following excretion, but the mucus evidently remains in the haustra of the colon for some time being moulded into various shapes by pressure from the hard fecal masses. The membranes are at times easily recognizable casts of secretions of the colon with the location of the follicles quite evident. They are transparent or opaque usually white in color but may be brown stained by the feces and occasionally red by blood. The wall of the membrane is laminated and bits of feces can be detected between the laminae. The diameter of the tube may reach one and one-half inches; the wall is usually thin, but may become greatly thickened. The membrane may be discharged as a solid ball alone or together with fecal masses and occasionally these masses may contain the mucus imbedded within or they may be surrounded by this secretion. As has already been noted the mucus is occasionally blood stained due to slight rupture of small vessels in the mucus membrane caused by the passage of hard fecal masses. Chemically the membrane consists mainly of coagulated mucin and not of fibrin as was formerly maintained. Microscopically, the membrane is found to be structureless and transparent and contains within bits of fecal matter, and undigested food fibres but is free from signs of inflammation. Only in advanced cases do we find fibrin, leucocytes, epithelial cells, many disintegrated micro-organisms, cholesterin crystals, and phosphates. Under higher magnification the inner surface of the membrane presents a reticulated appearance.

Intestinal Sand. The passage of intestinal sand is not of uncommon occurrence in mucous colitis, according to Hale White. It may not be observed until late in the course of this affection. It consists of reddish brown or yellow or black sand like granules, discharged in small or large amounts and is composed largely of the calcium soaps of palmitic and stearic acid and calcium phosphate in addition to urobilin and is probably formed in the colon. Intestinal sand observed in mucous colitis must not be confused with false sand produced by the ingestion of large amounts of bananas and pears.

The gastric contents reveals on examination a varied chemistry—achylia and hypochlorhydria are frequent findings though normal acidity and hyperchlorhydria are not uncommon. According to Von Noorden[9] of 20 cases examined 4 showed an achylia; in the others hyperacidity and sometimes subacidity was noted.

The gastric secretion was examined in 411 of our 500 cases. Normal acidity was found in 165 (40 per cent); hyperchlorhydria in 113 (27 per cent) and hypochlorhydria and achylia in 133 (32 per cent).

Symptoms and Signs of Minor Importance. Bockus, Bank and Wilkinson[7] have carefully studied their cases

String sign in lower bowel, involving the splenic third of the transverse colon. Note the spastic appendix.

of mucous colitis with reference to imbalance of the vegetative nervous system and concluded that in a larger proportion of instances there is an over excitability of both the parasympathetic and sympathetic systems, the former being most marked. In 32 of our cases in which basal metabolism observations were recorded normal findings were obtained in 19; decreased metabolic rate in 6 and increased in 7. These findings correspond closely with those of Bockus who likewise points to the absence of a generally decreased basal rate in his cases.

Of 310 of our cases in which blood pressure readings were recorded hypertension occurred in 32 per cent; hypotension in 39 per cent and normal tension in 29; figures which are also closely in accord with those of Bockus and his coworkers.

Such manifestations as sweating, chilly sensations, tremors, palpitation, urticaria, angio-neurotic edema, dermographism and migrainous attacks, as are noted by Bockus, were also prominent in many of our cases.

Diagnosis. Inasmuch as our methods of diagnosis have been much improved during recent years many cases of mucous colitis are now recognized which formerly escaped detection. In typical instances the diagnosis is unmistakable. The sudden onset of recurrent attacks of abdominal colic followed by the passage of membranes in individuals affected with chronic constipation renders the diagnosis simple. In those instances however in which the symptoms are atypical, there may be considerable difficulty in arriving at a correct conclusion.

This may occur especially during the first attack in which the pain may precede the discharge of mucus by a considerable length of time. On the other hand, however, attacks of mucous colitis may appear as apparently typical but may be caused by diseases of other organs and the underlying condition may be entirely overlooked. The attacks of pain may especially simulate such affections as renal colic, appendicular colic, biliary colic or the pain produced by a twisted ovarian cyst. A thorough examination, to which reference will be called later, will however usually lead to the correct diagnosis. It is interesting to note, that 82 of our cases had been subjected to abdominal operations. Of these 24 (28 per cent) received no apparent relief from the procedure. The operation consisted of appendectomies, cholecystostomies, cholecystectomies, release of adhesions and pelvic operations. The absence of the admixture of mucus with the stool does not necessarily indicate according to Strauss[20] the non-existence of a mucous colitis. In doubtful cases cleansing injections may be employed in order to demonstrate its presence.

Additional aid in diagnosis is obtained by means of sigmoidoscopic examinations, through which important information may be obtained. In the early stage of this affection the vessels of the bowel are greatly engorged, and the capillary injection is especially prominent, the mucus membrane being covered with a glairy mucus which gives an appearance similar to that of shad roe.

In the second stage in which the condition is more fully developed the

appearance is somewhat altered. There is no longer the intense engorgement of the membrane, nor do the vessels stand out prominently, neither the intense glairy appearance of the membrane, nor the marked increase of mucus covering the entire mucous membrane are observed; but distinct areas in which the mucous membrane is covered with a thick tenacious mucus which adheres closely and which at times can only be removed with difficulty. This condition gradually passes into the third stage in which the mucous membrane seems to be thinned out, pale, covered with mucus, and at times membranes are noted. When these membranes are removed small pin-head ulcerations are observed. These are not typical ulcerations but appear as though the mucus membrane is slightly denuded of its superficial surface. Following the removal of the membrane the mucosa gradually within a few days assumes a nearly normal appearance. Not uncommonly at this stage the mucosa may be observed covered in areas varying from three to four inches with membrane, in other areas with a tenacious mucus. It is an interesting fact that following removal of the mucus by washing with a solution of bicarbonate of soda that the mucosa appears almost normal. Remissions are not uncommon and last for a varying period of time during which the bowels assumes a perfectly normal appearance. If the disturbance progresses however, the mucous membrane may lose some of its resistance and we have noted after a long period of time in a number of instances actual ulcerations occurring as a final process with atrophic changes in the mucosa.

Spasm is not uncommonly noted in the bowel, occasionally to so marked a degree as to make the examination not only difficult but also extremely painful. The sigmoidoscopic examination is not only valuable as an aid in arriving at a diagnosis of this affection but is likewise extremely helpful in excluding associated conditions such as carcinoma. Sigmoidoscopic examinations were made in 438 of our cases and in these definite evidence of mucous colitis was present in 89 per cent.

The roentgen-ray furnishes important information in the diagnosis of mucous colitis and in obscure forms is often invaluable. The technic is followed as in the usual routine gastro-intestinal examination. Mucous colitis is best revealed from the twelfth to the twenty-fourth hour examination. The patient is required to return the morning following the administration of the barium meal and after a bowel movement if possible. Not infrequently following an action the roentgen signs are observed to the best advantage. If no bowel movement occurs only a very small area of the bowel may present the so-called "string sign" or there may be only spasm at hand with marked increase of the haustra. At times no roentgen evidence whatever will be noted in the examination. Spasm of the bowel is an early roentgen finding of this affection but occurs in so many other conditions that its significance is much lessened. At times a feathery appearance of the bowel is observed, most frequently noted in the descending colon. The

An unusual long string sign, involving almost the entire colon.

feathering of the colon simulates the appearance of the small bowel. The typical "string sign" which may be revealed at any stage is an extremely characteristic sign of mucous colitis. The fluoroscopic examination during the eighteen hour period does not always reveal these changes due to the small amount of the opaque meal in the bowel. At times the "string sign" is so thin and faint that it can only be determined on a well taken film. This occurs so frequently according to our experience, that we no longer rely on the fluoroscopic examination.

The "string sign" of mucous colitis is by no means always a constant finding. It may be observed at any portion of the colon, the most frequent site being in the descending colon; the transverse colon to a lesser degree. The ascending colon and cecum may also present this sign in rare instances. The calibre of the string line varies usually from one half to two mm. in diameter but may be larger in some instances. The line is usually straight and continuous, and as a rule presents no break in its full length. Very frequently the "string sign" begins with the feathery appearance for several inches and then tapers off into the string. According to Crane[21] the "string sign" is produced through the spasticity of the bowel undergoing certain peristaltic movements upon the mucoid material. It occurred in 10 per cent of our cases.

The routine barium colon enema does not always present much direct evidence; the meal flows up the colon readily and no abnormality of the lumen is noted under the fluoroscope; while in the film very frequently the descending colon will reveal an absence of haustra and at times some narrowing which is quite suggestive of a colitis. In our routine enema an immediate film is made of the colon and another film following the elimination of the barium. In the latter examination the string sign or feathery appearance of the colon will often be revealed in cases of mucous colitis. It has been observed according to our experience, even when the routine gastro-intestinal study was negative.

Kantor[22] has advised as a routine that a nine hour observation be made following the administration of the barium meal. At this period hypermotility of the intestinal tract will be noted, the barium appearing in the pelvic colon and rectum. This sign is however variable and may even occur in other conditions. In mucous colitis on the other hand due to the usual constipation as well as the marked spasticity of the colon, hypermotility is often not present. No abnormal roentgen changes were revealed in the cecum or ascending colon in our series. The ileum presented no eighteen hour residue or other abnormal changes. In addition the X-ray revealed ptosis of the colon in 58 per cent and spasm in 51 per cent of our cases. It further presented evidence of gastric ulcers in 3 per cent; of duodenal ulcer in 5 per cent; of chronic cholecystitis in 18 per cent of which 4 per cent were cases of cholelithiasis; of duodenal dilatation in 1 per cent, of chronic appendicitis in 24 per cent, and of diverticulitis in 1 per cent.

Differential Diagnosis. It is important to distinguish between the true forms of mucous colitis, and those

produced as secondary manifestations of other diseases of the bowel. Mucus in the form of membranes may be discharged for example in such conditions as cancer and ulcerative colitis.

On the other hand mucous colitis may simulate cholecystitis, appendicitis, peptic ulcer, intestinal polyps, carcinoma, diverticulitis, ulcerative colitis, renal colic and ovarian cyst with twisted pedicle.

When the hepatic flexure is mainly involved, the affection may suggest cholecystitis; when in the cecal region, appendicitis may be simulated and when in the transverse colon peptic ulcer. A careful physical as well as X-ray and proctoscopic examination will ordinarily lead to a correct diagnosis and prevent the serious error of advising unnecessary surgical interference.

Polyps, carcinoma of the bowel and diverticulitis can also be excluded by careful sigmoidoscopic and X-ray investigations. The differential diagnosis between mucous and ulcerative colitis is not always simple, especially when the ulcerations are of a mild type. A proctoscopic examination together with the examination of the mucus discharged is of the greatest importance in diagnosis. In the ulcerative forms there is a constant admixture with pus and frequently blood while in mucous colitis the mucus is free of blood and pus. When the ascending colon is mainly involved severe types of mucous colitis may simulate kidney colic. Here too, a careful examination of the urine, an X-ray of the kidneys and cystoscopic investigation on the one hand, and an examination of the stool, sigmoidoscopic as well as an X-ray investigation following a barium meal on the other, will usually lead to a correct conclusion. An ovarian cyst with twisted pedicle can usually be excluded by means of a careful pelvic examination.

Prognosis. The prognosis for complete recovery in mucous colitis depends largely upon the duration of the disease which may in some instances extend over many years. In early cases if treatment is promptly and carefully instituted recovery is to be expected. Of this type, Schmidt-Von Noorden[17] contend 90 per cent should entirely recover. In late cases however, and especially those in which secondary changes have occurred, the prognosis must be guarded. However, even in these, abdominal colic and discomfort may often be overcome and the patient be entirely relieved of annoying symptoms.

Relapses are common in all forms. According to Von Noorden[17] the prognosis is far less favorable in those instances not associated with constipation and relapses are here far more common.

According to the statistics of Von Noorden[9] of 76 cases treated complete success of treatment occurred in 79 per cent; incomplete success in 15.8 per cent, permanent success in 50 per cent, relapses in 13.1 per cent; unknown 15.8 per cent; failure in 5.2 per cent.

Treatment. In the treatment of mucous colitis it is obvious that the cause must as far as possible be first overcome. On this account, it is of the utmost importance, that a general as well as complete survey of the patient be undertaken. Focal infections of

whatever nature must be eradicated. The entire gastro-intestinal tract must especially be examined in order that any possible causative factor may be discovered and corrected.

If the theory be accepted, that mucous colitis has its origin in an imbalance of the vegetative nervous system and is therefore a purely functional affection, the method of treatment becomes evident. Inasmuch as the disease is observed in psychoneurotics, a careful analysis into the patient's emotions and mental state must be undertaken. Reeducation is essential in the cure of these invalids, and every effort should be made to alter the patient's attitude toward existing conditions. This is not always a simple matter, and not infrequently many prolonged consultations must be held before the patient's confidence is restored, and an insight gained in, to the true state of his condition. Unless he realizes, that his disability is purely functional and remediable largely through his own efforts but slight relief can be expected.

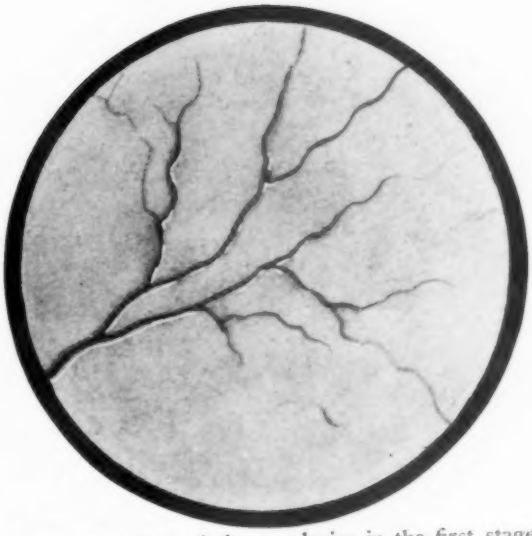
The constitutional factor must also be taken into consideration. The exhaustion of the nervous system which is the cause of the physical and mental fatigue still further depresses the already weakened constitutional defect. Consequently it is of the utmost importance for individuals affected with mucous colitis that overwork be avoided, and that a requisite amount of rest as well as diversion be obtained.

The regulation of the diet plays an important rôle in the treatment of mucous colitis. However, authorities have not been in accord regarding the character of the diet to be prescribed. Some as Von Noorden[8] advocate the employment of a diet containing large proportions of an indigestible residue with an excess of fat. According to this authority a cure can be more easily effected by rapidly overcoming the constipation brought about by this method of treatment. The food should consist mainly of bread containing an excess husks (graham bread), in addition to vegetables containing much roughage and fruit with seeds. As an essential feature of this method, Von Noorden advises that the change from a bland to this indigestible laxative diet should be brought about suddenly and not gradually; even though the symptoms become at first aggravated. As a result of a diet of this type the formation of hard stools is prevented and they become soft and abundant. The favorable effect of a diet of this type is attributed mainly to the large amounts of cellulose which it contains.

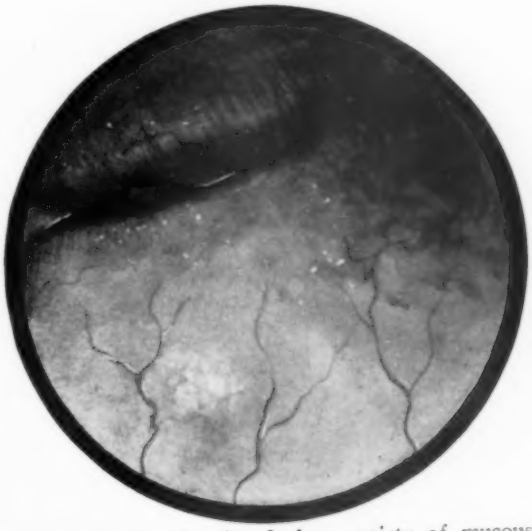
According to other authorities as Fleiner[23] and Schmidt[24] the diet should be so regulated as to protect and spare the bowel undue irritation as far as possible, and they therefore advocate the use of a bland non-stimulating diet producing but a small residue in the bowel. In order to overcome the tendency to the formation of extremely constipated stools Fleiner advises the systematic employment of retention oil enemata.

According to our experience any strict inelastic diet should not be prescribed. Under all conditions a rational diet based largely upon the needs of the individual is to be advised.

In general it is best at first to place the patient upon bland food, and grad-



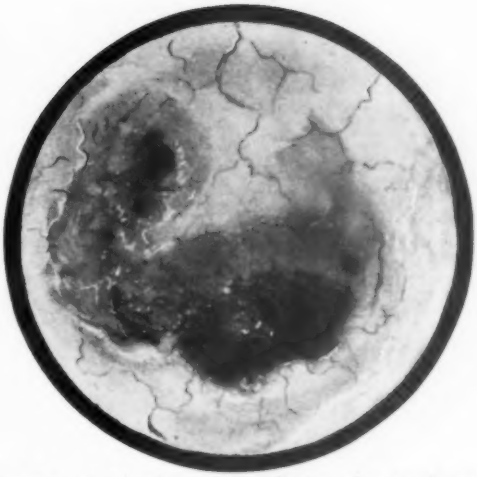
Shows dilatation of the capularies in the first stage.



Illustrates the first stage, showing the shadroe variety of mucous colitis, with acute manifestations.

Shadroe variety of mucous colitis; the appearance of the mucous membrane, overshadowed by mucus.

Illustrates the second stage, showing a plastic proctitis, with intense engorgement of the mucous membrane.



Shows the combination of the first and second stages.

Membranous or third stage; membrane rolled over to show the inflammatory condition of the bowel.

ually increase to a nutritious mixed and laxative diet, which should not be however too coarse. On a diet of this type the movements of the bowel usually become more normal and the secretion of mucus lessened. In the milder cases, a diet consisting largely of roughage may be prescribed at times at the onset with advantage.

In addition the food should be regulated with a view of overcoming certain underlying causes as well as contributing factors such as anemia, undernutrition and various digestive disturbances which may be at hand. In some instances the "smooth diet" of Alvarez[25] may be followed with advantage for a time.

The special management of a number of associated conditions require further consideration; of these colic, constipation and undernutrition are most important. With the onset of colic the pain may be so intense as to require immediate bed rest. Under all circumstances, it is important whenever the colic is frequent or is intense, that the patient be at rest until this symptom abates. The application of hot stupes to the abdomen usually affords considerable relief. In extreme cases, codeine, pantapon or even morphia may become necessary. At times benefit may be obtained from the administration of atropine hypodermically. In milder cases relief is often afforded by the use of enemata of hot water or of oil retained over night. In the early stages, the use of purgatives must be avoided.

The diet should be of the liquid and soft variety at this period and atropine or belladonna should be administered in adequate doses. In some instances in our experience great benefit is derived from luminal given in moderate doses (¼ grain) three or four times daily. The proper management of the chronic constipation so constantly present in mucous colitis is of extreme importance. Attention has already been directed to the dietetic measures so essential in the treatment of this symptom. In addition the use of acidophilus milk to which milk sugar may be added has been found useful. Cohnheim[26] has recently recommended the employment of bitter chocolate bars. Three to four ounces are to be consumed daily for this purpose. The patient is ordered one ounce in the morning before breakfast, and a similar amount at bedtime, to be followed by 3 to 4 ounces of water. In addition three quarters of an ounce is to be taken before luncheon and before dinner. In some instances one or two ounces per day is all that may be required for this purpose; in others five ounces may become necessary.

The oil enemata which are to be retained over night are extremely useful in regulating the bowel movements; in some instances the employment of saline or bicarbonate of soda enemata become essential. The indiscriminate use of purgatives is to be avoided. Castor oil is valuable at times, when administered at weekly intervals in doses of one half to one ounce or small doses may be prescribed to advantage given in capsules three or four times daily. Mineral oil and agar-agar are useful in some instances in regulating the bowels and olive oil taken in adequate amounts is invaluable for this purpose especially when

malnutrition exists. Not infrequently great relief may be obtained by a sojourn at mineral spas at which the water is recognized to possess a remedial effect in this affection. Of these Bedford, Saratoga and White Sulphur are useful examples in this country and Kissingen, Carlsbad, Marienbad, Vichy and Neuenahr in Europe. It is a well observed fact, that the cure of the constipation is likewise frequently followed by a cure of the colitis, which according to Schmidt and Von Noorden[17] indicates that the irritation of hard scybalous masses may have some bearing in the etiology of mucous colitis. On the other hand relief in this disease is by no means always noted by a cure of the constipation, and in many instances even when this symptom is effectively overcome, large quantities of mucus still continue to be discharged. Overcoming undernutrition is important in the relief and cure of this disease. In the aggravated types, in which there is marked loss of flesh and which are frequently complicated with marked grades of enteroptosis, well planned rest cures become essential. These should be directed not only toward building up of the physical condition of the patient by a gain in weight and improvement in the blood picture, but also in improving the state of the nervous system by means of psychotherapeutic measures. An increase in flesh and improvement in the general nutrition will also often markedly overcome long standing and severe types of mucous colitis and thus relieve the patient of depression and nervous fears. This treatment is best undertaken in a hospital or sanitorium, and should extend over a period of from four to eight weeks. Additional benefit may be obtained during this period from the judicious employment of hydrotherapy, heliotherapy, diathermy as well as from application of medicated stupes to the abdomen. In the enteroptotic patient the application of a well fitting abdominal support following the bed rest is of distinct advantage. In certain instances in which a gain in weight cannot be accomplished through forced feeding, this may be brought about as Frank[27] has recently pointed out, by the administration of insulin with the addition of adequate amounts of carbohydrates. Colonic irrigations with medicated solutions so commonly practiced in this condition are of extremely doubtful utility. The irritation of the bowel is apt to be increased by such measures and they are likewise harmful in further undermining the nervous system in these psychoneurotic individuals by centering the patients attention too closely upon his disability. Water or a weak solution of bicarbonate of soda in the form of irrigations may be helpful when employed once or twice weekly in some instances. In others great relief may be obtained from the instillation and retention of olive oil in the bowel over night, or of two ounces of a two to four per cent solution of protargol, or a five per cent gelatin solution, as has been recommended by Dudley Roberts.

Drugs play but a very unimportant rôle in the treatment of mucous colitis. Intestinal antiseptics are useless. Attention has already been directed to the value of castor oil as well as mineral oil for the relief of constipation.

Drastic purgatives should never be employed.

There are few other drugs of value in this affection. Atropin and belladonna in increasing doses are especially helpful in overcoming spasm. Such sedatives as valerian, the bromides and luminal are at times, exceedingly useful. Whenever there is an absence of hydrochloric acid or a diminution of this acid in the gastric secretion muriatic acid is indicated; while if hyperacidity is present alkalies should be administered. According to Bockus, Bank and Wilkinson, the use of calcium combined with parathyroid gland may be helpful in the treatment of this condition. Such surgical procedures as appendicostomy or caecostomy, which have been advised from time to time for the treatment of this affection are unnecessary and cannot be too strongly condemned.

Summary

Three views as to the nature of mucous colitis have been maintained: 1. That it is purely neurogenic and that the mucus produced is entirely a nervous hypersecretion; 2 that it is catarrhal in nature produced as the result of inflammation of the mucous membrane of the colon; 3. that it is partly neurogenic and partly inflammatory. The impression is gaining ground that in most instances at least there are inflammatory changes at hand even though these be of a mild type. There is no question, however, that this condition manifests itself mainly in individuals prepared by an instability of the nervous system. There is also sufficient evidence to indicate that this constitutional factor plays an important etiological rôle and that there is a correlation between the physical type and the secretory and motor disturbance.

As contributory factors associated with the development of this affection are chronic constipation, visceroptosis, cholecystitis, appendicitis, chronic disease of the female generative organs, endocrine disturbances, food allergy, abdominal adhesions, gastric and intestinal dyspepsia and focal infections.

Mucous colitis occurs most frequently in the female sex and is most common between the twentieth and fiftieth years. The usual symptom is chronic constipation associated with colicky pain and the passage of mucus in the form of membranes. The gastric contents reveals a varied chemistry, achylia and hypochlorhydria being most common. In typical instances the diagnosis is simple. Attacks of mucous colitis may, however, simulate other affections or may be secondary to other more serious disorders. Sigmoidoscopic and roentgen ray examinations are important as methods of diagnosis. The roentgen "string sign" is especially valuable in this regard though it is not constantly present.

In the treatment, it is important that the causative factors must as far as possible be overcome. Focal infections must be eradicated. The nervous system especially requires careful supervision. The diet must be carefully regulated though a strict inelastic diet should not be prescribed. A rational diet based largely on the needs of the patient is to be advised, which should be regulated to overcome the constipation, undernutrition and the various digestive disturbances which may be at hand. Colonic irrigations

are of doubtful utility and drugs play an unimportant rôle. Atropin or belladonna are of value in overcoming spasm. Surgical procedures are unnecessary and should not be undertaken.

REFERENCES

[1]Powell: Med. Trans. Royal Coll. Phys. London, 1820; Vol. 6; pg. 106.

[2]Mason Good: The Study of Medicine, Cl 1; Ord, 1; Species 7, Vol. 1. Phila., 1825; pg. 162.

[3]Fernelius: Patholog. Lib. 6, cap. 9, p. 181, Paris, 1854.

[4]Da Costa: Am. Jour. Med. Scien., 62, 371; 1871.

[5]Von Leyden: Deut. Med. Wochenschrift, 8; 44; 1882.

[6]Nothnagel: Diseases of the Intestines and Peritoneum, 2nd Edition. W. B. Saunders Co., 1907. page 233.

[7]Bockus, Bank and Wilkinson: Am. Journ. Med. Scien., 176; 813; 1928.

[8]Hurst: Constipation and Allied Conditions. Oxford Med. Public, 2nd Edition, 1919, page 282.

[9]Von Noorden: Membr. Catarrh of the Intestines. E. B. Treat & Co. N. Y., 1906, p. 54; 60; 41.

[10]Vaughan: Virginia Med. Mo., 49; 316; 1922.

[11]Duke: Arch. Int. Med., 28; 151; 1921.

[12]Andresen: Med. J. and R., 122; 271; 1925.

[13]Hollander: Amer. Jour. Med. Sci., 174; 495. 1927.

[14]Vaughan: South. Med. Jour., 21; 894; 1928.

[15]Bastedo: J. A. M. A., 92; 602; 1929.

[16]Norman and Eggston: New York Med. Jour., 116; 62; 1922.

[17]Von Noorden: Schmidt and Von Noorden Klink der Darmkrankheiten, 2 Auf. J. E. Bergmann, Wiesbaden, 1921; 333; 339; 343.

[18]Mallory: Jour. A. M. A., 90, 601; 1928.

[19]Boas: Archiv. f. Verdauunskr., 42; 270; 1928.

[20]Strauss: Deut. Med. Wochenschr., 49; 1568; 1923.

[21]Crane: Am. J .Roent. and Radium Ther. 17; 416; 1927.

[22]Kantor: Amer. J. Roent. and Radium Ther. 17; 405; 1927.

[23]Fleiner: Berl. Klin. Wochenschr., 30; 93; 1893.

[24]Schmidt: Klin. d. Darmkr., Auf. Bergmann, Wiesbaden, 1921, pg. 342.

[25]Alvarez: The Mechanics of the Digestive Tract. Hoeber; 1928, 2nd Edition, page 327.

[26]Connheim: Archiv. f. Verdauungskr., 42; 356; 1928.

[27]Frank: Deut. Med. Wochenschr., 53; 219; 1927.

The Principles Under-Lying the Calculation of Flexible Diabetic and Ketogenic Diets*

By Robert W. Keeton and Helen Mackenzie, *Chicago, Illinois*

THERE is a constant pressing demand by medical students, hospital internes and practitioners, who have not had a large experience in quantitative diet adjustment, for a simple and direct method of calculating diets. To be valuable, such a method must be adequate to meet the varying clinical situations presented. Many attempts have been made to answer this question. In most of those published, there is either a lack of flexibility, which handicaps one in dealing with the different clinical problems, or else a system of test diets is proposed which is applicable to classes rather than individuals. The present method allows one to calculate with equal ease a diet for a patient with an acidosis or one for a patient with a relatively mild diabetic defect. It treats the patient as an individual and offers a direct method of calculating the diet factors with a minimum of re-adjustment. It has been in use four years at the University of Illinois and has been very helpful in teaching the subject to medical students.

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The Total Calories in the Diet

Following the suggestion of Wilder,[1] an adult at bed rest is given either his basal requirements or basal plus 10%. An ambulatory patient is given basal plus 30%, and a patient at work, basal plus 50% to basal plus 75%.

This method was used by Campbell[2] and Ladd and Palmer,[3] and is now in general use. The nomographic chart of Boothby and Sandiford[4] for estimating the basal requirements, facilitates this calculation.

In the case of children there is less agreement as to the total calories to be fed. This is due to the absence of a definite method of measuring the calories necessary for growth and activity. In the case of infants and children below 7 years of age, confined to bed, Benedict and Talbot[5] estimate that during moderate activity the metabolism is 25% above the basal level. When the child is relatively quiet, the metabolism is 15% above basal. Something must be added for the specific dynamic effect of food, so a safe caloric level at which children below 7 years may be maintained during short periods of desugarization and diet adjustment, is basal plus 30%. After the child passes 7 years of age, Benedict and Talbot estimate that very

little is to be added for activity when the patient is confined to bed. The requirements then for such a child at bed rest, are approximately basal plus an increment for specific dynamic action of food. Hence these children may be safely maintained for short periods at basal plus 10% to basal plus 15%.

Benedict and Talbot have discussed the food requirements for activity. During bed rest and sleep (10 to 12 hours), the requirements are basal; during the time spent in the school room and devoted to moderate activity (6 to 8 hours), they are basal plus 75%; during the period of actual play (4 to 6 hours), there are no measurements available. In many children this requirement may be basal plus 200%; in others much less. Hence the total quantity of food prescribed will have to be determined by studying the child as an individual and by consulting statistical studies of food consumed by healthy growing children. The estimates of Holt and Fales[6] have made liberal allowances for activity based on such studies. By reference to Table II, it will be noted that the calories advocated by Holt and Fales correspond fairly closely to basal plus 100% on the basis of Benedict and Talbot's predictions.

Talbot and associates[7] in discussing the treatment of epileptic children advise the use of diets containing basal plus 50%. Ladd[8] finds that satisfactory growth occurs in diabetic children on diets 40% to 50% below the standards set by Holt and Fales. This corresponds to basal plus 50% to basal plus 60%, on the basis of Talbot's predictions. Bartlett[9] found that his children showed a positive nitrogen balance when the total calories of the diet approached those advocated by Holt and Fales. G. L. Boyd[10] in summarizing the caloric requirements for growth, considers that the use of Holt's standards are justifiable if the child be fed according to his theoretical rather than his actual weight. Julian D. Boyd and Nelson[11] used Holt and Fales' estimates of energy requirements, and found that their children grew rapidly in height and that they were in advance of the standards commonly used. They contrasted their results with those of Joslin, who fed only ½ to ¾ of the calories given to their cases. They stressed the value of liberal feeding in stimulating growth in height.

From the above discussion one may conclude that the diabetic child under restricted activity may be fed basal plus 30% for the purpose of desugarization. In view of the insistent teaching that diabetic patients should be kept at a low metabolic level, it would seem wise to feed a diabetic boy, who is being returned to activity, basal plus 75% on the basis of his theoretical weight. Under the same conditions a diabetic girl is to be fed basal plus 50% on the basis of her theoretical weight. Secondary adjustments may then be made as needed to maintain a normal growth curve. The basal requirements are taken from the predictions of Talbot[12] according to height.

The Protein Requirements

As a result of the studies of Sherman[13] in the normal subject, and Marsh Newburgh and Holly[14] in the diabetic, it has been generally accepted

that the adult patient may be maintained in satisfactory nitrogen equilibrium on 2/3 of a gm. of protein per kilo body weight. Emphasis also has been laid on the unfavorable effect on the diabetic defect of excessive quantities of protein. It is quite generally agreed that the protein in the adult diabetic diet should range between 0.66 gm. and 1.0 gm. per kilo body weight. It is also obvious that, if an adult should be given a ketogenic diet, the protein should be kept low so that the largest amount of carbohydrate may be given.

For the development of the method of diet calculation proposed in this paper, it became necessary to express the calories derived from the protein as a percentage of the total calories. Sherman[13] noted in his experiments that the protein calories necessary for maintenance of nitrogen equilibrium, constitute 6% of the total calories. Du Bois[15] has shown that the normal individual in the post-absorptive state develops approximately 15% of his energy from protein. An intermediate figure of 10% should furnish an adequate but not excessive quantity of protein.

In Table I a study is made of the grams of protein per kilo body weight in the case of men, which are furnished by diets containing basal plus 50% (diets for activity) and in which the protein calories constitute 10% of the total calories. It is obvious that when desugarizing diets of lower caloric value are used, the protein values per kilo also will be lower. In the first part of each table nine combinations of height and weight are considered in a patient of 30 years of age. In the second section of the table, three widely different ages of an individual of average size are treated. It will be noted that the grams of protein

TABLE I. GRAMS PROTEIN PER KILO

Protein Calories 10% *Total Calories* (M/40)

Men Age 30 Description		*Varying Size* Weight in Kg.	Basal B	B + 50%	GM of Protein	GM Protein Per Kg.
Short						
	20% Underweight	46	1300	1950	48.7	1.0
	Normal	57	1420	2130	53.2	0.9
5′	20% Overweight	69	1540	2310	57.7	0.8
Average						
	20% Underweight	55	1540	2310	57.7	1.0
	Normal	69	1700	2550	63.7	0.9
5′ 8″	20% Overweight	83	1840	2760	69.0	0.8
Tall						
	20% Underweight	67	1760	2640	66.0	1.0
	Normal	84	1960	2940	73.5	0.9
6′ 2″	20% Overweight	100	2100	3150	78.7	0.8
	Men 5′ 8″ *Normal Size*			*Varying Ages*		
Young	16 yrs.	62	1790	2685	67.1	1.1
Middle Age	40 yrs.	72	1700	2550	63.7	0.9
Old	65 yrs.	74	1620	2430	60.7	0.8

per kilo body weight fall below the value of one. By a similar computation these same relations may be shown to exist in the case of women.

If one should plan his diets on the basis of the theoretical weight for a given height rather than the actual weight, it will be noted that the protein value would reach 0.9 grams per kilo, which is sufficiently low to satisfy the demands of the advocates of low protein diets. It was therefore considered satisfactory to furnish the adult with a diet in which 10% of his total calories were derived from protein.

In the case of the child the problem is again complicated by the growth factor. Holt[16] states that healthy active children take 15% of their calories in the form of protein. He also states that 4 grams of protein per kilo body is taken in infancy and that this is reduced to 2 grams in adolescence. Bartlett[9] finds that the minimum protein for maintenance falls from 1.5 grams per kilo at 1 year of age to 0.6 grams at 14 years. G. L. Boyd[10] found that the minimum protein varied between 2.8 grams per kilo at 2 years to 1.25 grams at 10 years. This author states that for growth these values must be increased 10%. In diabetic children, Ladd[8] reported growth occurred in girls on diets which averaged 17.7% of calories from protein with a low value of 12.7%. Similarly boys grew on diets containing protein calories ranging from 12.1% to 20.8% with an average of 15.5%. Growth has occurred on levels of 1.5 to 2.0 grams per kilo. Talbot and associates,[7] Luther[17] and Peterman[18] in planning ketogenic diets have adopted 1 gram of protein per kilo body weight. As noted before the protein in these diets must be kept to the lowest limit compatible with health, so as to make the diet palatable.

Reference to Table II and III show that when 12½% of the total calories are fed as protein, and the more liberal caloric level of Holt and Fales is

Table II. Grams Protein per Kilo in Children

Protein Calories 12½% Total Calories (M/32)

	Boys				*Girls*			
	Holt & Fales		Benedict & Talbot Basal & 100%		Holt & Fales		Benedict & Talbot Basal & 100%	
Wt. in Kg.	Total Calories	Protein per Kg. Wt.	Total Calories	Protein per Kg. Wt.	Total Calories	Protein per Kg. Wt.	Total Calories	Protein per Kg. Wt.
3	360	3.8	300	3.1	360	3.8	300	3.1
5	590	3.7	540	3.4	590	3.7	570	3.6
10	990	3.1	1090	3.4	990	3.0	1080	3.4
15	1300	2.7	1450	3.0	1260	2.6	1380	2.9
20	1600	2.5	1720	2.7	1520	2.4	1610	2.5
30	2400	2.5	2230	2.3	2370	2.5	2090	2.2
45	3600	2.5			3330	2.3		
60	3720	1.9			2640	1.4		
68	3265	1.5						

adopted, the grams of protein per kilo body weight corresponds to the optimal amount of protein indicated by the statistical studies of Holt and by the results in treating diabetic children as recorded by Ladd[8] and Boyd.[10] In Table III the grams of protein per kilo body weight are shown, when the child is maintained at a somewhat lower level and the protein calories are estimated at 12½% of the total calories.

In Table IV the protein calories constitute 10% of the total calories, and the total calories correspond to basal plus 75% for boys and basal plus 50% for girls. The protein values derived in this table correspond more closely to those in use in the ketogenic clinics. Hence it is proposed that diabetic children be given 12½% of their calories in the form of protein, and that epileptic children under ketogenic management be given 10% or less of their calories as protein.

TABLE III. GRAMS PROTEIN PER KILO IN CHILDREN
Protein Calories 12½% of Total Calories (M/32)

	Boys			*Girls*		
Weight in Kg.	Basal	Basal + 75%	Protein Grams Per Kg.	Basal	Basal + 50%	Protein Grams Per Kg.
3	150	262.5	2.73	150	225	2.34
5	270	472.5	2.95	285	427.5	2.608
10	545	853.75	2.66	540	810.	2.84
15	725	1268.75	2.64	690	1035.	2.15
20	860	1505.	2.35	805	1207.5	1.85
30	1115	1951.25	2.03	1045	1567.5	1.63

TABLE IV. GRAMS PROTEIN PER KILO IN CHILDREN
Protein Calories 10% of Total Calories (M/40)

	Boys			*Girls*		
Weight in Kg.	Basal	Basal + 75%	Protein Grams Per Kg.	Basal	Basal + 50%	Protein Grams Per Kg.
3	150	262.5	2.18	150	225.	1.87
5	270	472.5	2.36	285	427.5	2.13
10	545	853.75	2.13	540	810.	2.02
15	725	1268.75	2.11	690	1035.	1.72
20	860	1505.	1.88	805	1207.5	1.5
30	1115	1951.25	1.62	1045	1567.5	1.3

THE GLUCOSE VALUE OF THE DIET AND THE KETOGENIC-ANTI-KETOGENIC RATIO

It is evident that if a diet must contain a certain number of calories and that if the protein calories are to compose a definite portion of these total calories, that the glucose of such a diet will then be fixed when a given ratio of fatty acids to glucose is selected.

The chief criticism which may be made to the various published[12 19 20]

methods of diabetic diet adjustment, is the fixed ratio of fatty acids to glucose. More recently Wilder[21] has developed a method of diet calculation which gives a varying ratio. However, his calculations are all based on a fixed protein value of 50 which presents some objections. If a relatively mild diabetic presents himself for treatment, one might desire to use a high fat ratio in order to desurgarize him rapidly without the use of insulin. If on the other hand, a case presenting a severe defect with an established ketonuria is encountered, it might be wiser to place the patient at once on a diet rich in carbohydrate (low fat ratio) and to supplement his tolerance with insulin. There are almost as many degrees of tolerance as there are patients. Hence it would be a great convenience to have available a simple method for calculating a diet with a ketogenic-antiketogenic ratio suited to the particular needs.

Evans[22] recognized this and proposed a method which allows one to pass from ratios of 1 to 4. However, he has to have a separate equation for the calculation of each constant. A simpler method would be more satisfactory. Ladd and Palmer[3] accomplished the same result by assuming that for all practical purposes the ketogenic amino acids in the protein molecule may be ignored. This same principle has been used in the calculation of ketogenic diets by Talbot, Metcalfe and Moriarity,[7] and Luther.[17] Perhaps the error involved in this assumption may not be great but it is nevertheless definite.

In one of his illustrative diets Woodyatt[19] observed that, if protein be taken as 1 gram per kilo body weight and the fatty acid to glucose ratio be taken 1.5, the calories were 17 times the glucose value of the diet. It seemed wise therefore to generalize this into an expression from which a constant could be obtained that would be applicable to any desired ratio.

Derivation of the Constant

The expression for this constant will be derived when the protein calories constitute 10% of the total calories. The basic assumptions are taken from Woodyatt's[19] discussion of the glucose and fatty acids in the diet.

The total calories (M) in the diet may be derived sufficiently accurately by multiplying the protein in grams (P) and the carbohydrate in grams (C) by 4, and the fat in grams (F) by 9.

$$(1)\quad M = 4C + 4P + 9F$$

The glucose (G) of the diet represents all the carbohydrate plus 58% of the protein plus 10% of the fat.

$$(2)\quad G = C + .58P + .1F$$

By transposing

$$(2a)\quad C = G - .58P - .1F$$

The fatty acids (F A) represent 46% of the protein plus 90% of the fat.

$$(3)\quad FA = .46P + .9F$$

By transposing and solving for F

$$(3a)\quad F = \frac{FA - .46P}{.9}$$

The ratio (R) equals the fatty acids divided by the glucose

$$(4)\quad R = \frac{FA}{G}$$

$$(4a)\quad FA = RG$$

The protein calories are 4 times the protein in grams but they are also 10% of the total calories.

Protein calories $= 4\,P$

Protein calories $= \frac{\text{Total calories (M)}}{10}$

$$4\,P = \frac{M}{10}$$

$$(5)\quad P = \frac{M}{10}$$

The constant which we are seeking is a number which, when divided into the calories in the diet, will give the glucose of the diet.

$$(6)\quad \frac{M}{K} = G \qquad (6a)\quad \frac{M}{G} = K$$

If now the value of C equation (2a) and P equation (5) be substituted in (1) we have:

$$M = \frac{4(G - .58M - .1F)}{40} + \frac{4M + 9F}{40}$$

By simplification:

$$M = 4G + .042M + 8.6F$$

On substitution of the value of F equation (3a) and F A equation (4a):

$$M = 4G + .042M + \frac{8.6(RG - .46P)}{.9}$$

On simplification and substitution of value P in (5):

$$M = 4G + 9.55RG - .0678M$$

$$M = \frac{G\,(4 + 9.55R)}{1.0678}$$

$$\frac{M}{G} = K = \frac{4 + 9.55R}{1.0678}$$

$$K \quad (10\%P) = 8.943R + 3.746$$

As will be shown later the value of K will be sufficiently accurate if this expression is simplified into:

$$K \quad (10\%P) = 9R + 3.7$$

When the protein calories constitute 12½% of the total calories then it can be shown by a similar analysis that:

$$P = \frac{M}{32}, \text{ and}$$

$$K \quad (12\tfrac{1}{2}\%P) = 8.803R + 3.687$$

or more simply

$$K \quad (12\tfrac{1}{2}\%P) = 8.8R + 3.7$$

Calculation of a Diet by Use of the Constant

The usefulness of this constant may be best seen by a specific example: A patient requires 2,000 calories and it is considered advisable to use 1.2 ratio:

$$K \quad (10\%P) = 9R + 3.7$$

$$K \quad (10\%P) = 9 \times 1.2 + 3.7 = 14.5$$

$$G = \frac{\text{Calories}}{K\ (\text{constant})} = \frac{2{,}000}{14.5} = 137.9 = 138$$

$$FA = G \times R$$

$$FA = G \times 1.2 = 165.6$$

$$P = \frac{M}{40} = \frac{2{,}000}{40} = 50$$

$$F = \frac{FA - .46P}{.9} = \frac{165.6 - 23}{.9} = 158.4$$

$$C = G - .58P - .1F = 138 - 29 - 15.8 = 93.2$$

Calories calculated 1,998.4.

Calories desired 2,000.

TABLE V. DIET FACTORS
P = M/40 and K = 9R + 3.7
(10% P)

R	G	FA	C	P	F	Calories Obtained	Calories Desired	Error in Calories
1	126.0	126.0	90.8	40	119.5	1599.1	1600	0.9
3	52.1	156.3	13.6	40	153.2	1593.6	1600	6.4
1	157.5	157.5	113.5	50	149.4	1998.9	2000	1.1
3	65.2	172.4	17.0	50	191.6	1992.1	2000	7.9
1	252.0	252.0	181.7	80	239.1	3198.2	3200	1.8
3	104.2	312.7	27.2	80	306.5	3187.6	3200	12.4

TABLE VI. DIET FACTORS
P = M/32 and K = 8.8R + 3.7
(12½% P)

R	G	FA	C	P	F	Calories Obtained	Calories Desired	Error in Calories
1	128.0	128.0	87.3	50.0	116.7	1599.3	1600	0.7
3	53.1	159.4	8.9	50.0	151.5	1598.4	1600	1.6
1	200.0	200.0	136.5	78.1	182.3	2498.9	2500	1.1
3	83.0	249.1	14.0	78.1	236.9	2500.8	2500	0.2
1	256.0	256.0	174.7	100.0	233.3	3198.7	3200	1.3
3	106.3	318.9	18.0	100.0	303.2	3201.2	3200	1.2

Reference to Table V shows that over a range of ratios from 1 to 3, and over a range of calories from 1,600 to 3,200, when K(10%P) = 9R + 3.7, the maximum adjustment is 12.4 calories. In Table VI over the same range when K(12½%P) = 8.8R + 3.7, the maximum adjustment is 1.3 calories.

It is therefore evident that by remembering the equation for the derivation of these two constants, a diet with any given number of calories and ratio may be simply and directly derived.

CALCULATION OF THE RATIO OF THE METABOLIZING MIXTURE DURING DESUGARIZATION

Another application of this method of calculation will be cited.

A patient enters the hospital showing a moderate ketosis. Certain questions arise. Can he be desugarized by diet adjustment alone? To what level must the glucose be reduced? Can such a desugarization be attempted with safety?

The basal requirements of the patient are 1,400 calories. This is the lowest level at which the weight can be maintained, and experience has shown that this quantity of energy will be completely used. We may then with confidence state that this is a close approximation of the calorific value of the metabolizing mixture. So the patient is placed on a diet of carbohydrate 60 gms., protein 35 gms., fat 113 gms., which yields a glucose of 91.6 gms., a fatty acid value of 118 gms., a ratio of 1.28 and calories 1,397. On such a diet he excretes 34 gms., 30 gms., and 32 gms., on successive days. The urine contains both acetone and diacetic

acid. His plasma carbon dioxide is 54. His average glucose excretion then is 32 gms. per day, and his present tolerance is (91.6 — 32) 59.6 gms.

We may now calculate the ratio of fatty acids to glucose in his metabolizing mixture.

$$\frac{\text{M (Total Calories)}}{\text{K (constant)}} = \text{G (Glucose)}$$

$$\frac{1400}{K} = 59.6$$

$$\frac{1400}{59.6} = K = 23.5.$$

$$9R + 3.7 = K$$

$$9R + 3.7 = 23.5.$$

$$9R = 19.8.$$

$$R = 2.2.$$

This should be a perfectly safe ratio. Wilder[1] and Shaffer[23] have shown that theoretically one molecule of glucose can catalyze the oxidation of two molecules of fatty acids or 1 gm. of glucose 3 gms. of fatty acids. Beyond this limit the diabetic organism cannot compensate for extra fatty acids which are produced and remain unburned. In other words a fatal acidosis will supervene.

It is an established plan in desugarizing by diet adjustment to reduce the glucose definitely below the patient's known or estimated tolerance. Hence the glucose in this case should be reduced to 50 gms. What would be the effect of such a reduction on the ratio? By a similar computation it can be shown that the ratio would now be raised to 2.7, which is just inside the maximal limit.

One may conclude that if the patient is not an arterio-sclerotic diabetic that he can be desugarized by reducing his glucose intake to 50 gms.; but that on such a diet the patient is called on to burn a metabolizing mixture, which contains a maximal quantity of fatty acids and for this reason the factor of safety in it is indeed small.

Conclusions

The principles underlying the calculation of flexible diets may now be summarized:

1. In adults the total calories fed during periods of desugarization vary between basal and basal plus 30%, and during activity between basal plus 50% and basal plus 75%. In children desugarizing diets should contain basal plus 30% calories. Diets adequate for growth and activity contain, in the case of boys, basal plus 75% calories, and in the case of girls, basal plus 50%.

2. In the adult the calories derived from protein constitute 10% of the total calories; in diabetic children, they constitute 12½% of the total calories. In children, under treatment with a ketogenic diet, the protein calories constitute 10% or less of the total calories.

3. When the protein calories are 10% of the total calories, an expression for a constant K was derived:

$$K = 9R + 3.7$$
$$(10\%P)$$

Now any desired value may be assigned to R (ratio) and the diet calculated by substitution in the expression:

$$\frac{\text{Total Calories}}{\text{K (Constant)}} = \text{Glucose}$$
$$(10\%P)$$

Once the ratio has been selected and the glucose calculated, the carbohydrate and fat can be easily derived.

4. When the protein calories are 12½% of the total calories, the expression for the constant becomes:

$$K\ (12\tfrac{1}{2}P) = 8.8R + 3.7$$

5. Such a constant is also helpful in computing the ratio of fatty acids to glucose, metabolizing at any given period during the process of desugarization.

6. Diets calculated according to these formulas give the desired calories without secondary re-adjustments.

BIBLIOGRAPHY

[1]Wilder, Russell M.: Optimal Food Mixtures for Diabetic Patients; Journal American Medical Association, Vol. 78, p. 1878, 1922. Optimal Diets for Diabetic Patients; Journal American Medical Association, Vol. 83, p. 733, 1924.

[2]Campbell, Walter R.: Diabetic Treatment in Diabetes Mellitus. Canadian Medical Association Journal, Vol. 13, p. 487, 1923.

[3]Ladd, William S. and Palmer, Walter W.: The Use of Fat in Diabetes Mellitus and the Carbohydrate—Fat Ratio. American Journal of Medical Sciences, Vol. 166, p. 157, 1923.

[4](May be purchased from H. N. Elmer, 53 W. Jackson Blvd., Chicago.)

[5]Benedict, F. G. and Talbot, Fritz B.: Metabolism and Growth. Carnegie Institute, Washington Publication No. 302, 1921.

[6]Holt, L. Emmett and Fales, Helen L.: The Food Requirements of Children. The Total Caloric Requirements. American Journal of Diseases, Vol. 21, p. 1, 1921.

[7]Talbot, Fritz B., Metcalf, Kenneth M. and Moriarity, Margaret E.: Boston Medical, Vol. 196, p. 89, 1927.

[8]Ladd, W. S.: Diabetes Mellitus and Growth. American Journal of Diseases of Children, Vol. 32, p. 812, 1926.

[9]Bartlett, W. M.: Protein Requirements as Determined in Diabetic Children. American Journal Diseases of Children, Vol. 32, p. 641, 1926.

[10]Boyd, G. L.: Treatment of Diabetes in Children. American Journal Diseases of Children, Vol. 29, p. 329, 1925.

[11]Boyd, Julian D. and Nelson, Martha V.: Growth Studies of Children with Diabetes Mellitus. American Journal Diseases of Children, Vol. 35, p. 753, 1928.

[12]Talbot, Fritz B.: Basal Metabolism of Children. Physiological Reviews, Vol. 5, p. 477, 1925.

[13]Sherman, H. C.: Protein Requirements of Maintenance in Man and Nutritive Efficiency of Bread Protein. Journal of Biological Chemistry, Vol. 41, p. 97, 1920.

[14]Marsh, Philip L., Newburgh, L. H. and Holly, L. E.: The Nitrogen Requirements for Maintenance in Diabetes Mellitus. Archives of Internal Medicine, Vol. 29, p. 97, 1922.

[15]Du Bois, Eugene F.: Basal Metabolism in Health and Disease. Lee & Febinger, Philadelphia.

[16]Holt, L. Emmett: Protein Requirements of Children. Archives Pediatrics, Vol. 38, p. 425, 1921.

[17]Luther, Eliot H.: The Treatment of Epilepsy with the Ketogenic Diet. The Modern Hospital, Vol. 28, p. 138.

[18]Peterman, M. G.: Epilepsy in Children. Journal American Medical Association, Vol. 88, p. 1868, 1927.

[19]Woodyatt, R. T.: Objects and Methods of Diet Adjustment in Diabetes. Archives of Internal Medicine, Vol. 28, p. 125, 1921.

[20]Hannon, R. R. and McCann, William S.: A Graphic Method for the Calculation of Diabetic Diets in the Proper Ketogenic—Anti-Ketogenic Ratio. Johns Hopkins Hospital Bulletin, Vol. 33, p. 128, 1922.

O'HARE, DWIGHT: A Chart for the Rapid Estimation of Woodyatt's Optimal Diabetic Diets. Journal American Medical Association, Vol. 78, p. 1124, 1922.

HOLMES, WILLIAM H.: Simplification of Woodyatt's Method for Calculating the Optimal Diabetic Diets. Journal American Medical Association, Vol. 78, p. 22, 1922.

BOYD, J. D.: The Use of Standard Diet Formulas in the Control of Juvenile Diabetes Mellitus. Journal American Medical Association, Vol. 87, p. 1020, Sept., 1926.

[21]WILDER, RUSSELL M.: A Primer for Diabetic Patients. W. B. Saunders Co., 1928.

[22]EVANS, FRANK A.: A Method of Establishing Diabetic Patients on High Calory Diets with a Ketogenic—Anti-Ketogenic Ratio Within the Limits of Safety. American Journal Medical Sciences, Vol. 166, p. 107, 1923.

[23]SHAFFER, PHILIP A.: The Ketogenic—Anti -Ketogenic Balance in Man and Its Significance in Diabetes. J. Biol. Chemistry, Vol. 54, p. 399, 1922.

Studies on the Diagnosis of Pancreatic Disturbances*

I. Methods of functional diagnosis

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THE present communication relates to the diagnosis of diseases of the pancreas. In it are reviewed the procedures and methods proposed as diagnostic aids and their status discussed.

Pancreatic disease has usually been considered as of infrequent occurrence. Cammidge (1) was one of the first to question its infrequency. In 1911 he wrote as follows: "Since 1900 it has been gradually recognized that chronic pancreatitis is a much more common disease than had been formerly supposed, but even yet there is a tendency to regard it as of theoretical rather than practical interest. This is far from being the case. My experience during the past ten years has convinced me that it is a very real disease and I feel sure that if it were more frequently diagnosed in the early stages, when treatment is of most avail, much needless suffering and even loss of life might be avoided. Its clinical importance lies not so much in its early symptoms as in the effects it may produce if allowed to progress unchecked."

Surgeons frequently diagnose the presence of pancreatic involvement by palpation during laparotomy. How much the surgeon can accurately determine concerning the state of the pancreatic gland through its palpation is an open question (2). Nevertheless, those of us whose work brings us into intimate contact with him soon learn that his palpating fingers possess a wonderful acumen in detecting pathologic anatomy within the opened abdomen. Whether or not Cammidge and other observers have been correct in diagnosing the presence of pancreatic involvement by the various methods employed by them also is admittedly an open question. Thus, the diagnosis of pancreatic disease is frequently based on evidence of uncertain status. However, it is at least suggestive enough to warrant further investigation.

A number of procedures have been proposed for the purpose of eliciting evidence of pancreatic involvement. Critical review of them demonstrates that they are designed to show functional disturbances in the pancreas either directly or indirectly through the secondary effects on metabolism. They may be classified as follows:

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I. Direct tests for pancreatic function.
   A. The estimation of the concentration of pancreatic enzymes in vitro (quantitative).
      1. Estimation in excreta
         (a) Trypsin in feces[3 4 5]
         (b) Diastase in feces[6 7 8]
         (c) Lipase in urine[9]
         (d) Diastase in urine[7]
      2. Estimation in gastric contents
         (a) Trypsin, diastase and lipase after an oil meal[10 11]
      3. Estimation of enzymes in duodenal contents[12 13 14 15]
      4. Estimation in blood
         (a) Diastase[7 16]
         (b) Lipase[17]
   B. The estimation of the concentration of pancreatic enzymes in vivo
      1. Keratin coated capsules containing methylene blue[18]
      2. Glutoid capsules of Sahli containing iodoform[19]
      3. Nucleus test of Schmidt,[20] and the modifications of Einhorn,[21] and Kashiwado.[22]

II. Test for demonstrating the secondary effects of pancreatic function on metabolism.
   A. Effect on carbohydrate metabolism.
      1. Glycosuria
         (a) Dynamic
         (b) Potential
      2. Cammidge pancreatic reaction[23]
   B. Unclassified effect on metabolism
      1. Loewi mydriasis test[24]
   C. Effect on alimentation
      1. Steatorrhea and percentage of undigested fats[2 25 26]
      2. Azotorrhea and creatorrhea[27 28]
      3. Urinary ethereal sulphates.

Only the basic principles of the methods above outlined are required for purposes of the present discussion. An intimate description of most of them will be found in the publications of Pratt,[2] Sladden,[27] Spriggs and Leigh,[18] Decker[28] and Wallis.[29]

Discussion of the Clinical Significance of Tests for Pancreatic Function; Direct Functional Tests in Vitro

Procedures proposed for the purpose of determining the action of pancreatic enzymes in vitro may be divided into two general classes as follows: (a) those which incorporate the proper physicochemical conditions governing enzymic action, and (b) those disregarding such conditions. Sörenson[30] has established the physicochemical conditions governing the activity of enzymes.

One of the few means for quantitating an enzyme is by determining its concentration. The concentration may be established indirectly by measuring the activity of the enzyme under a given set of experimental conditions. If the degree of activity is to be the index of an enzyme's concentration in different media, the method for estimating such activity must operate under the physicochemical conditions

which will produce the following phenomena: (1) uniformity of enzymic action; (2) proportionality of enzymic activity; (3) stability of the enzyme; and (4) homogenous physical state of the medium on which the enzyme is to act. A fifth important condition relates to the quantitative accuracy and delicacy of procedures for estimating the amount of enzyme action. The action of an enzyme is considered uniform when under a given set of experimental conditions similar results with a certain specimen containing the enzyme are obtained in repeated analyses. Uniformity of enzymic action is obtained by the proper concentration of hydrogen ions maintained by suitable buffer conditions. These same conditions govern proportionality of enzymic action, and unless they are proper the proportionality of enzymic action will be very slight. Obviously, the stability of an enzyme in relation to the length of time its action is to be measured must be considered in any method for demonstrating uniformity or proportionality of enzymic activity. This means that the action of the enzyme studied must be approximately as great at the conclusion of an experiment as it was at the beginning of the same, i.e., the concentration of the substrate must remain practically unaltered. The physical state of the medium on which the enzyme acts must be constant if uniformity of action is to be obtained. One essential reason for this is the fact that the size of the surface area of material exposed to enzyme action is an essential factor governing the amount of the latter. The proper physical conditions may be obtained by means of solutions or by emulsions so finely divided as partially to resemble colloidal suspension.

Hawk[8] used buffer salts in his method for determining the amylolytic concentration of stools. Unfortunately, all other methods described for estimating pancreatic enzymes in urine, stools or in gastric contents have disregarded buffer and hydrogen ion conditions. Disregard of these physicochemical conditions destroys proportionality of enzymic action; indeed it may permit a very low enzymic concentration to show more relative activity than one of much greater degree. Obviously, such results would lead to entirely erroneous clinical interpretation if the degree of activity is used as an index of enzymic concentration. Therefore, these methods are of insignificant clinical value. The method proposed by Hawk[8] for the estimation of diastatic concentration of feces would probably give good results were the procedure for determining the degree of action on the starch sufficiently accurate and delicate. In order to gain simplicity Hawk uses the well known Wohlgemuth[7] series of tubes containing starch. None of the chemical procedures necessary for determining accurately the concentration of the starch solution are used. Obviously therefore, the actual amount of starch acted on by the enzyme would be uncertain. Furthermore, relatively concentrated fecal extracts must be used, which destroys the delicacy of the method. Also, bacteria compose an appreciable proportion of feces. These bacteria give rise to enzymes which have the same action as those of pancreatic origin. These various factors detract greatly from the clini-

cal value of the results obtained by Hawk's method.

Except for the casein solution used by Gross[4] the substrata employed in determining either proteolytic (trypsin) or lipolytic (lipase) activity of urine, stools, or gastric contents have not been homogenous. Lack of homogeneity of such substrata permits tremendous variations in the degrees of activity of the enzymes. All the methods use procedures for determining the quantity of the product of enzyme action which are open to gross errors. The source of these errors are too apparent to necessitate their description. From this discussion it is obvious that the methods proposed for demonstration of pancreatic insufficiency by determining enzymic action in urine, stools and gastric contents can only give results of most uncertain reliability. Application of these methods to clinical medicine has been found to be of insignificant value by McClure and Pratt,[31] Pratt,[2] Spriggs and Leigh,[18] Wallis,[29] Sladden,[27] and others.

The determination of various enzymic concentrations of blood has been proposed as a means for estimating the activity of external pancreatic secretion. Wohlgemuth[7] applied his method for estimation of diastatic activity of urine to the blood. Unfortunately, here as in the urine, the method does not call for the use of buffer salts. Consequently enzymic action is not uniform and the results obtained give no conception of the true concentration of the diastase present in the blood serum. Obviously, clinical interpretation of such results can not be safely made. Myer[16] has devised a method for determining diastatic concentration of the blood. Chemically the method is correct except that the media used are not buffered. In view of the studies carried out by Sörenson[30] and of unpublished observations by Wetmore and McClure, it is doubtful whether uniformity of enzymic action of blood will be obtained in the absence of buffered solutions. This observation renders the results obtained by Myer's[16] method problematical.

Rona and Pavlovic[17] report that the activity of lipase of pancreatic origin is much less inhibited by atoxyl than lipase from other sources. On the basis of this observation they claim to have demonstrated pancreatic lipase in the blood, and propose its determination as an index to the activity of external pancreatic function. Kivilecki[32] has applied the method reported by Rona and Pavlovic clinically and concludes that it is of significance in the diagnosis of external dysfunction of the pancreas. However, the method proposed by these investigators does not incorporate those physicochemical conditions controlling enzyme action. Therefore, in spite of Kivilecki's conclusions, further investigations will be necessary before the clinical status of the procedure is established.

Einhorn[33] and Gross[34] have independently devised tubes by which contents from the duodenum can be obtained. Theoretically these contents could be examined for their enzymic concentrations and in this way one of the pancreatic external functional activities determined directly. Einhorn,[14] and Hollander and Mann[12] devised methods for the estimation of such

enzymic activities. However, their methods did not call for the use of buffered conditions and are open to the serious objections previously discussed. Bassler[13] devised a relatively simple method for the estimation of the concentration of the diastase present in duodenal contents. Unfortunately, the procedure for quantitating the end result is the inaccurate one proposed by Wohlgemuth,[7] while the solutions are improperly buffered. Furthermore, the highly important proteolytic and lipolytic functions of the pancreas are not determined. Obviously, it would be unsafe to rely on results obtained by this method, except perhaps in the presence of far advanced disease of the pancreas.

Recently Okada, Sakurai, Imazu and Kuramochi[15] have proposed new methods for estimating concentration of the enzymes of duodenal contents. They employed ether, alcohol, water and hydrochloric acid as stimulants to the secretion of pancreatic juice. These stimulants were used possibly because Okada and associates were apparently uninformed concerning the extensive investigations of McClure and coworkers[35 36 37 40 42] on the mechanisms of pancreatic stimulation. The latter have established beyond all reasonable doubt that in man adequate amounts of the products of the digestion of foodstuffs are the *only* substances which will *uniformly* stimulate the flow of pancreatic juice. Therefore, the specimens of duodenal contents analysed by Okada and coworkers represented the enzymic concentrations common to the fasting state plus whatever additions occurred as the result of widely variable degrees of pancreatic stimulation.

The Japanese investigators further conclude that 94 to 99 per cent of contents of the duodenum can be regularly collected through the duodenal tube by suction. However, McClure and Reynolds[37] made numerous observations which demonstrated conclusively that material can be aspirated from the duodenum only when the suction is applied coincidentally with the occurrence of duodenal peristalsis. Fluoroscopic observations showed that materials entering the duodenum quickly passed the duodenal tube, so that only indefinite amounts could be recollected through the tube either by siphonage or aspiration. These observations showed that aspiration has no advantage over siphonage. Furthermore, the method employed by the Japanese investigators for estimating the amount of material recollected through the tube was a colorimetric one, based on the determination of the concentration of phenolphthalein. The admixture of bile present in duodenal contents destroys the accuracy of such a determination. The physical conditions governing the proper use of the colorimeter are such that all solutions to be compared must be absolutely clear and of the same shade of color. Any juggling of the solutions in order to make the shades similar, as was done by the Japanese workers, can only lead to the grossest errors. Therefore, the method used by them does not ascertain what proportion of the contents of the duodenum can be collected through the duodenal tube. These observations show the futility of their attempts to estimate the

amounts of enzymes secreted by the pancreas from calculations involving the total amounts of duodenal contents.

McClure and Wetmore, as a basis for their work on duodenal enzymes, made extensive studies on the physicochemical conditions governing uniformity and proportionality of the action of such enzymes. These studies included observations on phosphate mixtures representing wide ranges of molecular and hydrogen ion concentrations. During such studies it was demonstrated conclusively that the ultimate molecular concentrations of phosphate mixtures proposed by Okada and associates do not produce either uniformity or proportionality of enzymic action.

The Japanese investigators did not locate the position of the duodenal tube by radiographic means before collecting duodenal contents for analysis. Material indistinguishable in its physical appearance from duodenal contents has often been obtained from the pyloric end of the stomach by the present author. Such observation demonstrates the impossibility of ascertaining the source of material returned through the duodenal tube unless the exact position has been determined fluoroscopically.

The data presented above demonstrate that the results obtained by the methods and procedures proposed by the Japanese investigators are subject to uncontrolled variables. The variables which most adversely affect the reliability of the results are as follows: (1) variable degrees of stimulation of the flow of pancreatic juice; (2) variability of calculated enzymic concentrations due to differences in the proportionate amounts of duodenal contents; (3) variability of enzymic action due to absence of physicochemical conditions producing uniformity and proportionality of such action; and (4) variable sources of the duodenal contents, from either the stomach or the duodenum. Obviously, all these variables render the results obtained highly difficult of interpretation. The effects of the variables discussed were observed by Okada and associates, but their cause was apparently not recognized. They attempted to overcome them by collecting duodenal contents over a period of three hours. They were apparently unaware that McClure and coworkers[36, 37] demonstrated that, when the proper pancreatic stimulants are used, the various hourly fractions of duodenal contents collected throughout periods of 5 and 6 hours give comparable results.

From the above discussion it is obvious that all the methods and procedures discussed for estimating pancreatic functional activity through determination of enzymic action give results which are of highly problematical value.

Direct Funtional Tests in Vivo

Capsules which contain chemicals, that appear in the urine after absorption from the intestine, have been proposed as tests for pancreatic function. Such capsules are coated with some substance resistant to gastric digestion but which may be dissolved by action of pancreatic juice. The two best known capsules are the keratin coated capsule containing methylene blue and the formalin hardened gelatin capsule

containing iodoform. However, the recent widespread use of coated pills and capsules for x-ray purposes serves to demonstrate how frequently such capsules or pills are not broken up in the small intestines. This observation renders highly problematical the significance of results obtained by the pancreatic test capsules. In actual practice this has been found to be the case by Wallis,[29] by Sladden,[27] by Spriggs and Leigh,[18] and Pratt.[2]

The sajoidin test of Winternitz depends upon the splitting up of an iodized oil in the intestines and the subsequent elimination of iodine in the urine. The theoretical value of this test was based on the assumption that the iodine would not be liberated in the absence of pancreatic juice. However, McClure, Vincent and Pratt,[20] showed that fats are split up in the intestines in the complete absence of pancreatic juice. This renders the utility of the sajoidin test very doubtful. The cube beef test of Schmidt consists of feeding beef in a muslin sac, recovering it from the stools and examining the degree of nuclear preservation. This test is of clinical significance in the complete absence of pancreatic juice. Einhorn,[21] and Kashiwado[22] have made minor modifications of the test. The nuclear test is, therefore, the only one of those designed to show pancreatic enzymic action in vivo which is of practical utility.

Tests Demonstrating Metabolic Disturbances

Glycosuria, the Cammidge[23] pancreatic reaction, Loewi's[24] adrenalin mydriasis test and the observation of increased ethereal sulphates in the urine are phenomena common to disturbances other than involvement of the external secretory function of the pancreas. This factor is sufficient to render difficult their interpretation in relation to affections of the pancreatic parenchyma. Nevertheless, glycosuria and the Cammidge reaction are occasionally of some value in deciding the question of destructive lesions of the pancreas.

In the absence of jaundice, grossly fatty stools are indicative of extensive disease of the pancreas or of marked pancreatic dysfunction; such as occurs in congenital steatorrhea. In creatorrhea, large amounts of microscopically well preserved muscle fibers, and azotorrhoea, high nitrogen content of the stools, are also present, then the condition is almost certainly one of very far advanced pancreatic insufficiency. At such a time the stools may show a large percentage of undigested fat. However, in the presence of marked disease of the pancreas,[27] or in its entire absence,[20] analysis may demonstrate little disturbance in fat digestion. Therefore, the absence of excess fat in the stools does not rule out the presence of pancreatic dysfunction. The proper examination of stools requires a complete metabolism experiment. This includes analysis of food ingested, collection of feces over a period of several days and their ultimate chemical analysis. Such an extended investigation is rarely of sufficient clinical value to be justifiable.

The following conclusions may be safely drawn from the foregoing discussion of the various pancreatic functional tests proposed:

1. All methods discussed for the estimation in vitro of enzymic concentration of urine, stools, blood and duodenal contents are subject to serious chemical and physico-chemical omissions of such nature that results obtained by them are difficult if not impossible of exact clinical interpretation.
2. The demonstration of the absence of pancreatic trypsin in vivo by the nucleus test of Schmidt is of practical utility in far advanced pancreatic disease. The capsule and iodized oil tests are of insignificant value.
3. Examination of the stools by the methods outlined are of practical utility in the diagnosis of conditions representing far advanced pancreatic dysfunction. Glycosuria and the Cammidge reaction are occasionally of practical value as indirect symptoms of external pancreatic involvement. The other methods for showing disturbances in metabolism secondary to pancreatic insufficiency are of doubtful utility.

The foregoing discussion shows the need for means of certainly ascertaining both minor and advanced degrees of disturbances in the state of pancreatic function. One of the most promising means for obtaining information concerning an organ's functional condition is the study of that organ's secretions. The digestive secretion of the pancreas is found in the duodenum, from which it may be obtained by means of the usual tube. McClure and coworkers have devised procedures for obtaining suitable specimens of duodenal contents and methods for their analysis. In order to obtain duodenal contents containing pancreatic juice representative of that secreted during the intestinal digestion of food it was necessary first to establish the usual physiologic mechanisms concerned in the stimulation of the external functional activity of the pancreas. The investigations[36] carried out on these mechanisms demonstrated that the products of food digestion were the usual stimulants to the secretion of pancreatic juice. In the course of animal studies it was demonstrated that, under suitable experimental conditions, introduction of the products of food digestion into either the femoral or mesenteric veins would stimulate the secretion of pancreatic juice. These observations on animals fully confirmed those made on man. Of the various food products, cream[37] or oleic acid[38] has been found most suitable for use in the procedure developed for collecting specimens of duodenal contents for analysis. The use of oleic acid permits examinations of the bile moiety[42] as well as of the pancreatic fraction. The state of the alkali secretory function of the pancreas is estimated as the buffer values of duodenal contents. The activity of the enzyme secretory mechanism is estimated by determining the concentration of three pancreatic enzymes present in duodenal contents.

The buffer values[39] of duodenal contents are determined by use of the potentiometer. Fifty cc. of the contents are titrated with tenth normal hydrochloric acid or sodium hydroxide solution, according to whether the original material was alkaline or acid. The re-

sulting pH values are determined up to and beyond the neutral point. Curves of these values are plotted against the amount of acid or alkali, and the amounts needed to bring the pH value to 7 are read from the curves. Further buffer values are computed from the equation developed by Van Slyke:

$$B = \frac{\triangle B \text{ or } \triangle A}{\triangle pH}.$$

$\triangle B$ or $\triangle A$, is the amount of tenth normal alkali or acid required to neutralize 1 cc. of duodenal contents; or

$$\triangle B, \text{ or } \triangle A = \frac{V : N}{\overline{V}} \text{ in which } V$$

is the volume of the alkali or acid used; N is the normality of the solution, and V the total volume of the original duodenal contents in the titration vessel. The total change in the pH value from the original to the neutral state is $\triangle$ pH. Methods[40] have also been devised for determining the enzymic concentration of the pancreatic fraction of duodenal contents. These methods incorporate all the chemical and physico-chemical principles which insure delicacy, uniformity and proportionality of enzymic activity. Also, the procedures for the estimation of the amounts of enzyme action give accurate results. Uniformity and proportionality of enzymic activity have been obtained by regulating the latter with phosphate mixtures. The amount of enzyme action for the proteolytic and amylolytic enzymes is estimated by application of the methods of Folin for nonprotein nitrogen and sugar in the blood. The activity of the fat splitting enzyme is estimated by determining the degree of acidity developed in a true emulsion of olive oil or of cottonseed oil, by titrating while hot with alcoholic potash solution, using phenolphthalein as an indicator. The delicacy of the methods is such that the enzymic concentration of 0.02 to 0.04 cc. of duodenal contents is determined.

Initial observations[36 37] on normal subjects established the activities of the pancreatic enzymes present in duodenal contents. Later these observations were fully confirmed by studies made by Jones.[41] Subsequent to the work of Jones, the author has added confirmation to all these observations by a study of a much larger series of control observations.[42] The results of studies[43] made on enzymic activities of duodenal contents in patients with unquestionable disease of the pancreas, many of whom came to autopsy or laparotomy, established the clinical value of such determinations. The results of these studies were confirmed later by observations[42] on a much larger number of patients. Sufficient numbers of observations have been made definitely to eliminate the various sources of error which were theoretically objectionable. When the proper portion of duodenal contents has been collected and the analytical methods have been correctly performed the results obtained give uniformly reliable information concerning the external secretory activities of the pancreas.

When the enzymic concentrations of duodenal contents is used as the index of activity of the external func-

tions of the pancreas, such concentrations fall into three groups as follows:

1. Normal concentrations are found in all conditions in which the functional activity of the pancreas is unimpaired.
2. Abnormally low concentrations are found in lesions including the ampulla of Vater, lesions involving the head of the pancreas and in acute or chronic pancreatitis.
3. An intermediate value between normal and abnormally low concentrations is characterized by normal concentrations of one or two enzymes, while that of the other one or two is much diminished below the minimum normal; that is, dissociation of the secretion of the various types of enzymes occurs. This is found in convalescence from acute pancreatitis, in functional impairment accompanying partial occlusion of the ampulla of Vater and also during stages of destructive lesions involving the pancreas. Jones[41] demonstrated such dissociation in diabetes mellitus.

McClure and coworkers therefore have established the following:

1. The usual physiologic mechanisms concerned in the stimulation of the digestive activities of the pancreas.
2. Procedures for obtaining duodenal contents representative of pancreatic juice secreted during intestinal digestion.
3. Methods of determining with a high degree of accuracy the states of activity of the enzyme and alkali secretory functions of the pancreas.
4. Physiological variations of the enzymic and alkali functional activities of the pancreas.
5. Variations in the enzymic concentrations in the duodenal contents in the presence of abnormal pancreatic function.
6. A clinical status for the results obtained by the use of the procedures and methods for determining the enzymic concentrations of duodenal contents.

By the use of these methods and procedures pancreatic dysfunction can be ascertained in its incipiency, as well as when far advanced.

Summary and Conclusions

Most tests designed to estimate the activity of the pancreas are based on erroneous physical and physico-chemical conditions. These conditions are so erroneous as to render the tests almost valueless. The nuclear test and certain metabolic examinations are of value in demonstrating far advanced disease of the pancreas. The presence of glycosuria and a positive Cammidge pancreatic reaction in the urine are of varying degrees of diagnostic aid. McClure and coworkers have devised means for accurately demonstrating pancreatic dysfunction of both mild and advanced degrees.

REFERENCES

[1]Cammidge, P. J.: Chronic pancreatitis, with special reference to the diagnosis and treatment. London Lancet, 1911, I, 1,494.

[2]Pratt, J. H.: The functional diagnosis of pancreatic disease. Am. Jour. Med. Sc., 1912, N. S. 143, 313.

[3]Müller, E., and Schlecht, H.: Ueber die Prüfung der Pankreasfunktion durch Trypsinbestimmungen in den Fäzes, Med. Klin., 1909, 5^1, 573.

[4]Gross, O.: Die Wirksamkeit des Trypsins und eine einfache Methode zu ihrer Bestimmung. Arch. f. exper. Pathol., 1907-08, 58, 157. Ibid, Deutsch. Med. Wnschr., 1909, 35, 706.

[5]Papp, C.: Ueber eine neue Methode zur Diagnostik der gestörten Pankreasfunktion. Med. Klin., 1926, 22^1, 257.

[6]Müller, E.: Die Starkekleisterplatte, ein einfaches Hilfsmittel zum Studium diastatischen Fermentwirkungen. Zntrlbl. f. inn. Med., 1908, 29^1, 385.

[7]Wohlgemuth, J.: Ueber eine ueue Methode zur quantitativen Bestimmung des diastatischen Ferments. Biochem. Ztschr., 1908, 9^1, 1 and 10. Ibid, Berl. Klin. Wnschr., 1910, 47^1, 1910.

[8]Hawk, P. B.: A modification of Wohlgemuth's method for the quantitative study of the activity of the pancreatic function. Arch. Int. Med., 1911, 8, 552.

[9]Opie: A case of hemorrhagic pancreatitis. The occurrence of a fat splitting ferment in urine. Johns Hopk. Hosp., Bull., 1902, 13, 117.

[10]Volhard, F.: Ueber die Untersuchung des Pankreassaftes beim Menschen und eine Methode der quantitativen. Münch. Med. Wnschr., 1907, 54^1, 403.

[11]von Ehrmann, R.: Ueber eine Methode zur Funktionsprüfung des Pankreas. Berl. Klin. Wnschr., 1912, 49^2, 1363.

[12]Hollander, E., and Marcus, J. H.: Pancreatic function. I. The quantitative determination of pancreatic enzymes. Arch. Int. Med., 1925, 36, 585.

[13]Bassler, A.: A quantitative test of digestive pancreatic activity, easily applied clinically. Arch. Int. Med., 1925, 35, 162.

[14]Einhorn, M.: Agar tubes for the estimation of pancreatic ferments. Med. Record, 1912, 82, 650.

[15]Okada, S., Sakurai, E., Imazu, T., and Kuramochi, K.: Pancreatic function: I. The quantitative estimation of pancreatic secretion. Arch. Int. Med., 1928, 42, 270.

[16]Myer, V. C.: Studies on animal diastases. I. Increased diastatic activity of the blood in diabetes and nephritis. Jour. Biol. Chem., 1917. 29, 179.

[17]Rona, P., and Pavlovic, R.: Ueber die Wirkung des Chinins und des Atoxyls auf Pankreaslipase. Biochem. Ztschr., 1922, 130, 225, and 1922-23, 134, 108.

[18]Spriggs, E. I., and Leigh, A. J.: A case of pancreatic insufficiency. Quart. Jour. Med., 1915-16, 9, 11.

[19]Sahli.: Ueber Glutoidkapseln. Deutsch. Med. Wnschr., 1897, 23, 6.

[20]Schmidt, A.: Ein Neues diagnostisches Merkmal bei Pankreas-Erkrankungen. Verhandl. d. Kongr. f. inn. Med., 1904, 21, 335.

[21]Einhorn, M.: Studien mit der Perlen-Probe zur Funktionsprüfung des Verdauungsapparates. Arch. f. Verdauungskr., 1907, 13, 475.

[22]Kashiwado, T.: Ein Beitrag zur Kernverdauung und eine Vereinfachung der Schmidt'schen Kernprobe zur Erkennung von Pankreasachilie. Deutsch. Arch. f. Klin. Med., 1911, 104, 584.

[23]Cammidge, P. J.: An improved method of performing the "pancreatic" reaction in urine. Medico-Chirurg. Transact., 1906, 89, 239.

[24]Loewi, O.: Ueber eine neue Funktion des Pankreas und ihre Beziehung zum Diabetes Mellitus. Arch. f. exper. Pathol., 1908, 59, 83.

[25]Müller, F.: Untersuchungen über Icterus. Ztschr., f. klin. Med., 1887, 12, 45.

[26]McClure, C. W., Vincent, B., and Pratt, J. H.: Absorption of fat in partially and completely depancreatized dogs. Jour. Exper. Med., 1917, 15, 381.

[27]Sladden, A. F. S.: Critical review: The diagnosis of pancreatic disease. Quart. Jour. Med., 1902, 7, 455.

[28]Decker, H. R.: The recognition of pancreatic insufficiency with special reference to the Loewi test. Bost. Med. & Surg. Jour., 1917, 176, 867.

[29]Wallis, M. R. L.: The diagnosis of diseases of the pancreas, with special reference to diastase in the urine. Quart. Jour. Med., 1920-21, 14, 57.

[30]Sörensen, S. P. L.: Enzymstudien (Fortsetzung). II. Mitteilung. Ueber die Messung und die Bedeutung der Wasserstoffionenkonzentration bei enzymatischen Prozessen. Biochem., Ztschr., 1909, 21, 201.

[31]McClure, C. W., and Pratt, J. H.: A study of diastatic activity of urine and feces, with special reference to diseases of the pancreas. Arch. Int. Med., 1917, 19, 568.

[32]Kivilecki, D.: Ueber den Nachweis atroxylresistenter Lipasen in menschlichen Blutserum bei Erkrankungen des Pankreas. Arch. f. Verdauungskr., 1926, 37, 336.

[33]Einhorn, M.: A practical method of obtaining the duodenal contents in man. Med. Record, 1910, 77, 98.

[34]Gross, M.: A duodenal tube. Jour. Am. Med. Assoc., 1910, 54, 1365.

[35]McClure, C. W., Jones, C. M., Wetmore, A. S., and Reynolds, L.: Studies in pancreatic function. The enzymic concentrations of duodenal contents in health and disease. Am. Jour. Med. Sc., 1924, 167, 649.

[36]McClure, C. W., and Wetmore, A. S.: Studies in pancreatic function. Enzyme concentration of duodenal contents after the ingestion of pure food mixtures by normal men. Bost. Med. & Surg. Jour., 1922, 187, 1. McClure, C. W., Montague, O. C., and Campbell, L. L.: Studies on the mechanism of external pancreatic secretion. Bost. Med. & Surg. Jour., 1925, 192, 527.

[37]McClure, C. W., Wetmore, A. S., and Reynolds, L.: Physical characters and enzymatic activities of duodenal contents. Findings during normal digestion in normal young men. Jour. Am. Med. Assoc., 1921, 77, 1468.

[38]McClure, C. W., Mendenhall, W. L., and Huntsinger, M. E.: The evaluation and treatment of disturbed liver function. Jour. Am. Med. Assoc., 1925, 85, 1537.

[39]McClure, C. W., Montague, O. C., and Campbell, L. L.: The pH and buffer values of duodenal contents derived from normal men. Arch. Int. Med., 1924, 33, 525.

[40]McClure, C. W., Wetmore, A. S., and Reynolds, L.: New Methods for estimating the enzymatic activities of duodenal contents of normal man. Arch. Int. Med., 1921, 27, 706.

[41]Jones, C. M., Castle, W. B., Mulholland, H. B., and Dailey, F.: Pancreatic and hepatic activity in diabetes mellitus, the alterations with some observations on the etiology of the disease. Arch. Int. Med., 1925, 35, 315.

[42]McClure, C. W.: The clinical application of the pathologic physiology of the external secretions of the liver and pancreas. Amer. Jour. Med. Sc., 1928, 176, 309.

[43]McClure, C. W., and Jones, C. M.: Studies in pancreatic function. The enzyme concentration of duodenal contents in pathological conditions involving the pancreas, liver and stomach. Bost. Med. & Surg. Jour., 1922, 187, 909.

The Treatment of Acute Asphyxia*

By Cecil K. Drinker, *Boston, Massachusetts*

THE subject I have to speak about is one of which I have had an exceptional chance during the past five or six years to become familiar with, and one which in its acute aspects the medical profession usually meets after something or other has been done by laymen.

Acute asphyxiations in the registration area of the United States cause about 14,000 deaths a year. The principal conditions in which acute asphyxia occurs are drowning, which makes almost 7,000 of these deaths, carbon monoxide poisoning, which makes about 6,000 more, and electric shock, which completes the total.

I want to speak first of all about carbon monoxide poisoning, in which I have been particularly interested. In 1920, at the request of the American Gas Association, I formed a commission to study methods of resuscitation from carbon monoxide poisoning. I was greatly surprised by the amount of such poisoning in fatal form which occurs in our large cities. In New York City, for example, exclusive of Brooklyn, the emergency service of the New York Gas Company is called to an average of 1,600 cases of carbon monoxide poisoning a year, with about 800 fatalities. Somewhere in the neighborhood of 45 per cent of these are suicidal. In practically every instance they are seen by laymen before a physician is called, but as soon as the physician reaches the case, he is in entire charge, and all other agencies are subservient to him.

It is an interesting commentary on the knowledge of the medical profession of the actual condition of persons who are seriously asphyxiated either from carbon monoxide poisoning, drowning, or electric shock that I have in my possession the records of nine cases where physicians have pronounced the individual dead. In two cases he turned the body over to the coroner, and in almost every instance fellow workmen continuing efforts of artificial respiration have succeeded in bringing back a complete recovery.

It is quite obvious that most physicians are not familiar with the degree to which circulatory activity can continue to persist in an individual in a very restricted area for a fair period of time and under circumstances which, with the finger and a stethoscope, are almost entirely beyond methods of detection.

If one takes the course of a case of carbon monoxide poisoning, certain interesting things happen which are related very directly to the method of treatment to be applied. When one breathes a low concentration of carbon monoxide, let us say a quarter of a per cent of carbon monoxide gas in the air of a room—and for your information, in order to have some basis

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for comparison the ordinary Ford car running in a closed garage, producing from 7 to 9 per cent of carbon monoxide in the gas in the exhaust, will develop an atmosphere which should be fatal within 5 to 6 minutes.

There is invariably a period of hyperpnea of varying length, depending on the rate at which poisoning occurs. During this period of hyperpnea with the individual wholly quiescent, carbon dioxide is progressively lost, so that the individual is projected slowly, fairly slowly, usually, into a condition of alkalosis. The CO_2 comparing power of the blood may be reduced after such a period, owing to the fact that bicarbonate has diffused from the vessels into the tissues. He is, however, in spite of this loss of alkali from the blood, in a condition of alkalemia. He is slowly moving over into a position in which respiratory stoppage is more or less inevitable.

What the cause of hyperpnea in carbon monoxide poisoning is certainly cannot be said with final assurance. It does not seem justifiable to me to attribute it wholly to the development of anoxemia. However, we find as the breathing begins to fail an individual, he is not only walled off from oxygen by the combination of carbon monoxide with his hemoglobin, but is in a position to help himself practically not at all as regards the intake of oxygen from the air. On the basis of this situation, Dr. Henderson and his co-worker Haggard recommended as their share of the work of our commission that these individuals be given an inhalation of carbon dioxide in order to supply the carbon dioxide which had been breathed out, and to stimulate breathing in a natural manner. With this carbon dioxide, following the very old method treatment, 95 per cent of oxygen was combined. The individual's breathing was thus stimulated by carbon dioxide and he took such a high concentration of oxygen as to increase the oxygen in his alveolar air and to hasten the disassociation of the carbon monoxide hemoglobin in the best manner possible. That treatment was put in actual operation in the United States in 1923. It is now possible to say that in practically all the large and many of the small cities in the country this mixture of 95 per cent oxygen and 5 per cent carbon dioxide can be placed at the disposal of physicians, usually by the local gas or electric companies who keep apparatus suitably designed and approved for us by a commission now in existence on the part of the American Gas Association, so that the apparatus may be safely used by the lay crews who are handling them.

In a case of carbon monoxide poisoning, which is reached soon by a physician in any one of the large cities, this simple physiological method of treatment can be reached at once. In New York City, for example, there are six, twenty-four-hour emergency stations so equipped, all within the call of anyone who may need such help. Here in Boston and vicinity the same is true, and so it goes throughout the country.

This treatment of gas asphyxiation, physiologically grounded, is apparently ideal, yet it has not succeeded quite as well in some instances as it should. The reason for this was not apparent to us until the past year. If one takes a group of normal subjects and has them breathe a mixture of 5 per cent

carbon dioxide and air, he finds to his surprise that every individual increases his minute volume to a different degree and at a different rate. We have known clinically that this occurred in certain degree in hypertension with arteriosclerosis, but the degree of variation which exists between different individuals and the rate and extent to which they increase their breathing when confronted with 5 per cent carbon dioxide certainly was quite unfamiliar to me. More interesting than this, and contrary to the literature as it now exists, the same individual breathing this mixture on different days responds quite differently. Let us speak of experiments within the past couple of weeks. For example, I myself breathing 5 per cent Co_2 increased my minute volume to 41 liters on one day. Five days before that, under conditions of health, as far as I could see, identical, my breathing increased to but 23 liters per minute. Therefore, when one takes 5 per cent carbon dioxide in apparent good health, for reasons which as yet are unexplored, the extent of the response in different individuals is quite different and the extent of the response in the same individual, contrary to past opinion, varies from day to day. While it is by no means proved, and probably extremely difficult to prove, it seems to me that this result indicates a variation in the threshold of the respiratory center for stimulation. That is to say, an equivalent hydrogenized concentration acting as the stimulating agents of the respiratory center operates with different degrees of vigor at different times in the same apparently healthy individual.

It is an interesting fact that if animals are given carbon monoxide to breathe and their response as asphyxia from the carbon monoxide develops, in terms of increased breathing to 5 per cent carbon dioxide inhalation, is measured, that as the asphyxiation progresses the response of the individual rapidly tends to decrease, so that in the most serious conditions of poisoning, when we really require stimulation of breathing, we have an individual whose threshold for stimulation has fallen and we have found that it is essential to begin the inhalation on such persons with a higher concentration. Seven to ten per cent is now being tried in the field, with very interesting results, and results in accord with some of the recent work on the inhalation of high concentrations of carbon dioxide in patients in catatonic states. I now have records of several cases with a return of consciousness, actual speech, on 7 per cent carbon dioxide. With a shift to the 5 per cent of carbon dioxide oxygen application, you will have a lapse into unconsciousness again after a few minutes, with a further recovery when put upon the higher concentration. It is thus evident that in the treatment of carbon monoxide poisoning the concentration of carbon dioxide used, as these cases reach the hospital and inhalation treatment is frequently available, should be increased and freely increased when the men are first seen by the physicians in charge.

Other details in regard to treatment with drugs are of little importance. I may mention only one very necessary precaution into which I cannot go into detail: It is that atropin is a decidedly dangerous drug for such individuals.

The Use of Sodium Salt of Dehydrocholeic Acid (Decholin) as a Choleretic*

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NEUBAUER has been foremost in the investigation of a sodium salt of dehydrocholeic acid that would stimulate the liver to increased formation of bile. Most investigators have shown this drug to be practically without toxic effects and that it markedly increases the flow of bile. Our investigation was undertaken to see if we could obtain results comparable to those reported by Neubauer, Rusznyâk and others.

Drugs that would increase flow of bile were sought by ancient medical investigators. The term cholagogue which was used to designate drugs that increase the flow of bile came into use between the time of Hippocrates and Galen, but Galen made the term popular. From the time of Galen until the experimental work on the liver by Claude Bernard, medical men were content to use their so-called cholagogues and fallaciously to measure results obtained by changes in the color of the feces.

About the time modern research had shown that most of the so-called cholagogues were ineffectual in increasing the production of bile Brugsch and Horsters originated the term choleretic to designate a drug which increases the flow of bile from the liver as distinguished from the term cholagogue which means expulsion of bile from the gallbladder.

Experiments on the content of bile began with the development of modern chemistry. In 1833, Demarçay separated three substances from bile which were probably bile acids. Ten years later (1843) Strecker isolated glycocholeic and taurocholic acid and showed their relation to cholic acid. From this time on chemists have been very active in this field of research. To illustrate, Viihland received the Nobel prize last year for his work on the structure of cholic acid.

As soon as chemists began to isolate and prove relationships of the various compounds of the bile acids the pharmacologists began to administer these compounds to animals. It was soon found that bile acids and many of their compounds actually increased the flow of bile. In general, the administration of bile acids and their salts has been disappointing because they may be toxic. At the present time, however, there is a sodium salt of dehydrocholeic acid which is not toxic when given in doses of from

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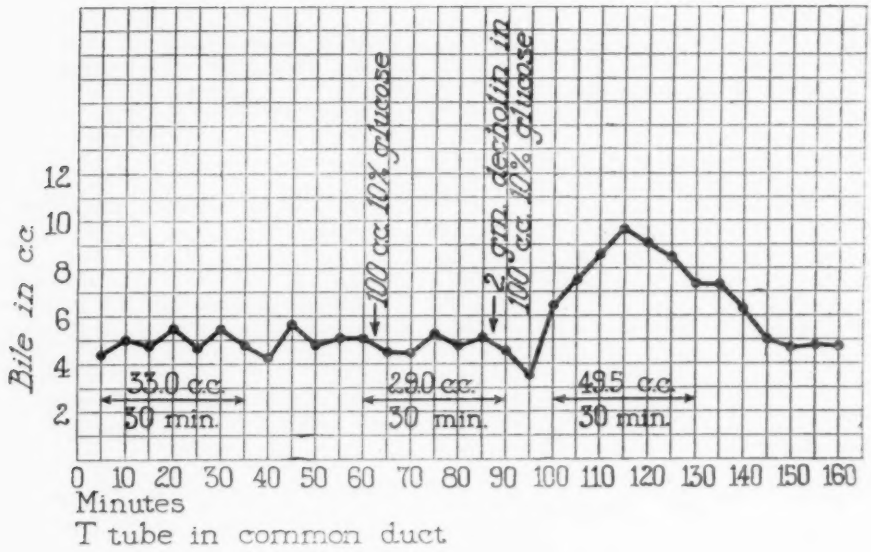
0.5 to 2.0 gm. (intravenously). This salt is prepared in aqueous solution, sterilized and put in ampules ready for use. It is sold under the trade name of "decholin."

Our observations were made on three groups of patients. In the first group external biliary drainage had been established with a T-tube in the common bile-ducts with a tube to the outside. In the second group the tube in the gallbladder opened to the outside; in this group the common bile-duct was completely occluded by a pancreatic neoplasm. In the third group the patients had not been operated on and were selected after it had been shown that a free flow of bile could be obtained with a duodenal bucket and tube.

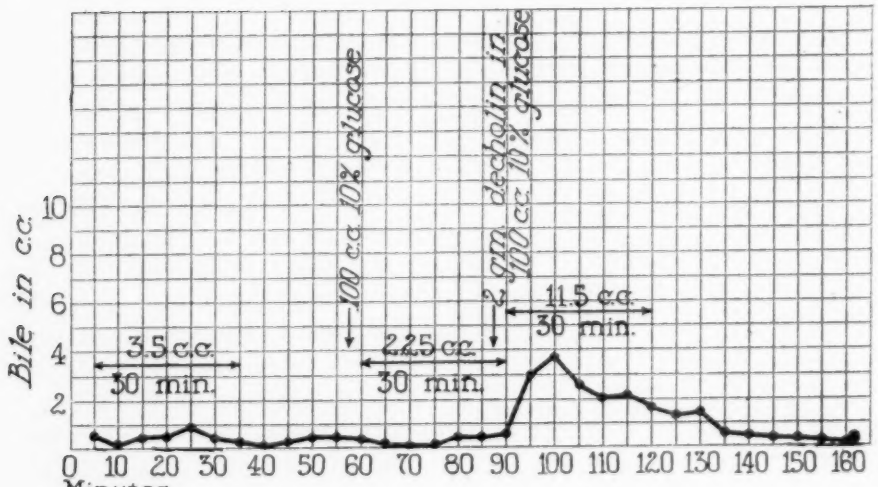
In a general analysis of the results it may be stated that all the experiments were begun about two hours after a meal, usually the noon meal. As far as possible a constant flow of bile was obtained. Frequently this took considerable time because patients with external bile drainage often had plugs of debris in the tubes which had to be removed by suction. In each experiment a period of one hour with an uninterrupted flow of bile was obtained before proceeding. This time is designated as the first control period. At the end of this period 100 c.c. of 10 per cent glucose was given intravenously. This was done to determine the effects on the flow of bile of giving 100 c.c. of fluids because we wanted to give the decholin diluted to a volume of 100 c.c. Following the glucose the second control period was begun which lasted thirty minutes. At the end of this period the decholin diluted to 100 c.c. with 10 per cent glucose was given.

The bile was collected in five-minute periods throughout all the experiments. During the experiments the patients remained quietly on the back or right side or in the same position during the entire time. That is, changes in the position were carefully guarded against.

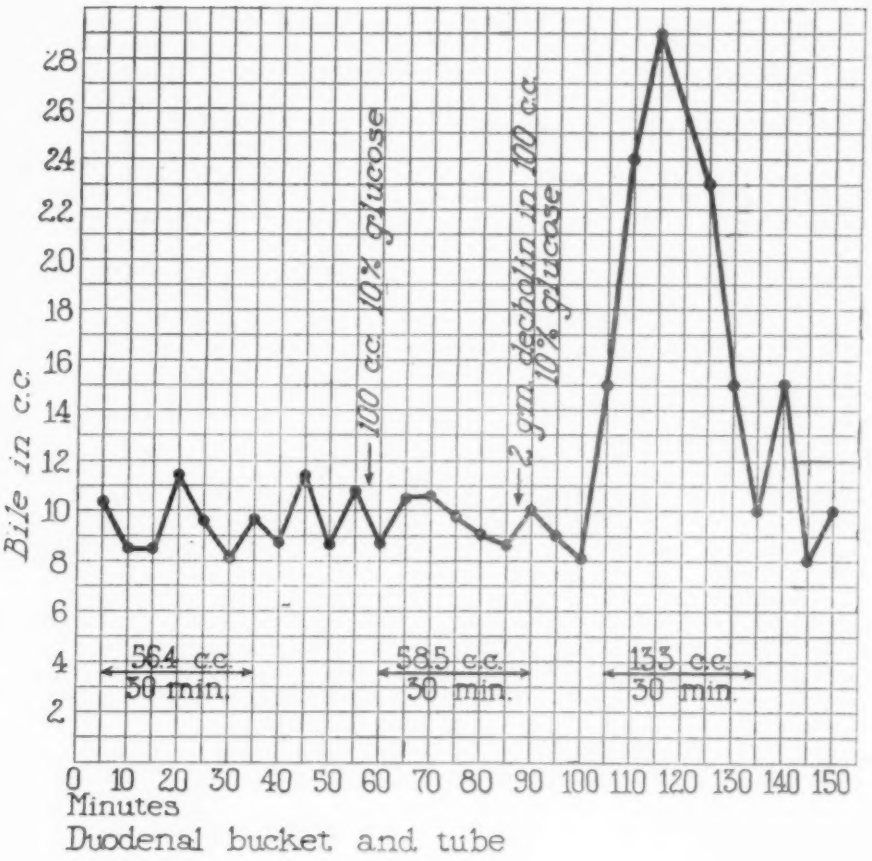
In an analysis of the curves (figs. 1, 2 and 3) certain definite points may be noted. The action of the drug is very prompt; in practically every instance the increase of the flow of bile was within fifteen minutes and in many instances the increase began much more promptly. The variations in the length of time before the increase in the flow of bile began cannot be attributed to the technic and time which it took to administer the drug. All the injections were made with size 18 needles and finished within a period of not more than five minutes. Some of the responses which were delayed more than ten minutes might have been due to plugs of debris in the tubes. At a casual glance one notices that there is a variation in the amount of increase in different patients (table 1). The peak of maximal response varies somewhat (figs. 1, 2, and 3 and table 1). It is possible that some of the delayed maximal responses were also due to debris and mucous plugs in the tubes. In practically every instance of external biliary drainage during the time the flow of bile was increasing there was a constant shower of mucous plugs and debris. The increase in the flow of bile was usually over within an hour after administration.



T tube in common duct.



Tube in gallbladder



In table 2 are shown some of the physical and chemical changes which take place in the bile. In order to make such studies it was necessary to pool the bile collected for ten or fifteen minutes before, during, and after the action of the drug in order to have sufficient quantities to work with. At the period of maximal choleresis the color of the bile was less intense. The bile salts, bilirubin and cholesterol were decreased relatively and absolutely. There was no definite change in the specific gravity. The dried weight increased.

It seems that the natural occurring constituents of the bile are diluted and at the same time the specific gravity is approximately maintained. The total solids are increased. Perhaps this can be accounted for by assuming that it is the decholin being excreted in the bile which keeps up the specific gravity. The values for the total solids are of little significance in a fluid which contains as much debris from tubes and varying amounts of mucus as bile.

TABLE 1

COMPARISON OF VOLUMES OF BILE EXCRETED DURING THE FIRST AND SECOND CONTROL PERIODS AND DURING THE HEIGHT OF THE ACTION OF DECHOLIN*

Cases	Bile at thirty-minute intervals, c.c.		
	First control period	Second control period	Height of action of decholin
Tube in gallbladder			
1	8.5	9.0	18.5
2	28.0	27.0	49.0
3	3.0	1.5	16.0
4	17.0	22.0	58.0
Tube in common bile-duct			
5	14.5	12.0	27.0
6	56.4	58.5	133.0
7	44.0	58.5	129.5
8	3.0	5.0	17.5
9	17.5	15.0	26.0
10	19.5	14.0	30.5
11	38.5	30.0	56.0
Duodenal tube and bucket			
12	39.5	35.0	120.0
13	21.0	25.5	41.0
14	13.0	10.0	80.5
15	30.0	40.0	75.0
16	10.5	10.0	9.5
17	8.5	7.0	8.0

*Results shown in the curves are not included in this table.

COMMENT

We have not determined the normal choleretic action of decholin because a patient cannot be considered normal if it has been necessary to put a T-tube in the common bile-duct or a tube in the gallbladder. A duodenal tube and bucket is the only direct means of determining increase in the flow of bile in the normal person, and this is beset with uncontrollable errors. Some of the bile is swept away from the bucket and the bile collected is probably diluted with gastric and duodenal contents. Evidence of toxic effects were watched for and none was observed; it should be noted, however, that in all of the patients employed there was a free flow of bile, either naturally or induced by artificial means.*

*McVicar intended to carry this work further. Since, by his death, he was prevented from publishing further reports, we append this note. In the course of work not connected with the present report, the drug was given to two subjects in whom the flow of bile was not free. In both, the concentration of serum bilirubin promptly rose. In one of them, who had a stone in the common duct, the injection was followed by pain.

TABLE 2
CHANGES IN THE CHEMICAL AND PHYSICAL PROPERTIES OF THE BILE BEFORE, DURING AND AFTER THE ACTION OF DECHOLIN

	Color	Volume, c. c.	Bile salts, mg. per cent	Bilirubin, mg. per cent	Specific gravity	Dried weight, gm.	Cholesterol		
							Bloor I	Bloor II	Split
Before	Dark amber	10	580.0	16.4	1.012 1.015 1.018	0.0573	65.0	69.0	4.0
During	Light amber	29	191.0	6.4	1.018 1.010 1.012	0.6120			
After	Amber	10	113.3	3.75	1.012 1.014 1.014	0.0208	30.0	30.0	

SUMMARY

We have been able to repeat the work of various investigators on the choleretic action of decholin. It has been found to be nontoxic in the doses given in patients in whom the flow of bile was free. The change which takes place in the bile seems to be one of dilution of the normally occurring constituents. An increase in the flow of bile was obtained in eighteen of twenty cases.

BIBLIOGRAPHY

[1]BRUGSCH, THEODOR and HORSTERS, HANS: Cholerese und Choleretica. Klin. Wchnschr., 1923, ii, 1538-1539.

[2]DEMARÇAY, HORACE: Quoted by Legg.

[3]LEGG, J. W.: On the bile, jaundice, and bilious diseases. New York, Appleton and Co., 1880, p. 157.

[4]NEUBAUER, ERNST: Dehydrocholsaure, ein wirksames, praktisch ungiftiges Glied der Gallensäuregruppe. Klin. Wchnschr., 1923, ii, 1065-1067.

[5]NEUBAUER, ERNST: Über die Cholagoge Wirkung der Dehydrocholsäure beim Menschen., Klin. Wchnschr., 1924, iii, 883.

[6]RUSZNYAK, STEPHAN: Die Wirkung des Dehydrocholsauren Natriums (Decholin) beim Menschen. Ztschr. f. d. ges. exper. Med., 1927, lvii, 537-553.

[7]STRECKER, ADOLPH: Untersuchung der Ochsengalle. Ann. d. chimie u. pharm., 1848, lxv, 1-37; lxvii, 1-60.

Fatal Purpura Complicating Chronic Interstitial Nephritis*

By Oscar Berghausen, B.A., M.D., *Cincinnati, Ohio*

PURPURA hemorrhagica is frequently accompanied by changes in the kidney and the suprarenal glands. The kidney may show evidences of hemorrhagic nephritis or only slight degenerative changes in the tubular epithelium with numerous foci of intertubular and intratubular hemorrhage. Little[1] cites four cases in infants and young children with hemorrhage into both suprarenal capsules proving rapidly fatal, and in which purpura was noted before death. At the post-mortem the chief finding was the hemorrhage into the capsules, the kidneys showing no changes beyond occasional hemorrhages. He also cites two very remarkable cases in which there was hemorrhage into both suprarenal capsules, not associated with other purpuric manifestations, and four cases of hemorrhage into one suprarenal capsule proving more or less rapidly fatal, but not associated with other purpuric manifestations.

Stevens and Peters[2] list a series of twenty-five cases of hematuria associated with clinical evidences of acute hemorrhagic nephritis. When it was possible to obtain the kidneys, they were found much enlarged and congested. Minot[3] states that chronic nephritis, arterio-sclerosis, and the debility of old age may be accompanied by simple symptomatic purpura and very rarely by symptomatic purpura hemorrhagica. He further adds that the change which occurs in the blood of these patients with chronic nephritis which permits bleeding, is unknown, and that the platelet count and coagulation time are usually normal. He cites a case of purpura developing in a girl following an attack of scarlet fever at the age of eight. Chronic nephritis developed and during the last fifteen years of her life she had intermittent bleeding from the stomach, gums, nose, and uterus, death occurring at the age of forty-five from cerebral hemorrhage.

Silver[4] reported an interesting case of purpura occurring in a tailor aged 52, who from the age of 27 suffered with headache, nausea, vomiting and purpuric spots all over the body. At the autopsy, there were evidences of extravasations of blood into many organs, the spleen was small and shrunken, the liver cirrhotic and fatty, the right kidney contained a cyst about the size of a walnut in the upper pole and filled with bloody grumous fluid. The capsules of the kidneys were somewhat adherent, the surfaces of

*From the Medical Service, Good Samaritan Hospital, Cincinnati, Ohio.

both organs were granular and the cortical portions pale. The weight of the kidneys was 11¼ ounces.

The following case report is that of a patient seen for the first time two weeks before her death. The diagnosis of purpura had not previously been made. When first seen, she was exsanguinated, delirious, and would readily lapse into a comatose state. The blood examinations showed the presence of secondary anemia and platelets were abundant in the smear. Four days after the first transfusion, the platelet count, the bleeding and coagulation time were within normal limits. Duke[5] states that the life of platelets is but a few days, so that the above normal findings cannot be ascribed to the transfusion of 500 c.c. of citrated blood. He noted that the platelets of normal individuals introduced into three patients having purpura hemorrhagica, disappeared within a period of about three days. Because of the blood examination, the diagnosis of simple symptomatic rather than hemorrhagic purpura was made. The patient was evidently suffering from uremic manifestations which are rare in true purpura hemorrhagica. Upon her admission to the hospital, twenty-five ounces of urine were obtained by catheter, but thereafter she voided from eight to twelve ounces during the day, as nearly as could be determined. The urine was pale, of low specific gravity and no casts were reported. Unfortunately, chemical examinations of the blood were not made. Considering the markedly contracted and sclerotic kidneys, which stripped of their fatty capsules weighed only 43 and 48 grams each, or 91 grams together, the purpuric manifestations were considered as secondary to the interstitial nephritis, probably founded upon some infection suffered earlier in life.

History of Case: Mrs. H. B., a white woman, aged 37, gave a history of having felt weak and indisposed for the past year. She was able to get about until two weeks before her admission to the hospital, or four weeks before her death. She had suffered from chills and sweating spells during the past year and had lost one hundred pounds in weight. She had been able to eat all types of food, but had vomited frequently for the past six months; the vomitus consisted of a clear watery fluid and occurred every morning. The remainder of the day she usually felt well. There was no jaundice and no blood in the stools. Occasionally she experienced pain in the lower abdomen. The menstrual periods had always been regular until the past four or five months when she noticed at times that she would menstruate twice a month. At times she would flood profusely. The personal history was negative except for a previous appendectomy. She had two children living and well, one died at birth. Her husband was living and well, and gave no history of venereal disease.

For the past two weeks she suffered from increasing dyspnea; she had been coughing considerably. The feet had been swollen for the past two years. During the past few days she had been vomiting more frequently than before; at times the vomitus contained blood. About two years ago she urinated frequently at night, as

many as eight or ten times. She drank large quantities of water. The nocturia gradually disappeared and during the past week she did not have to get up to void. There were no changes in the bones or joints. She had constant headache with radiating pains in the spine. There was some visual disturbance; at times she had diplopia and again she would be scarcely able to see.

The patient was large, still quite obese; acutely ill, very dyspneic, temperature 99, pulse 90, respiration 24. The skin was dry, loose, and showed several large purpuric spots over the back and thighs and upper extremities. The nail beds and mucous membranes were markedly anemic. The pupils were small and reacted to light and accommodation. The sclerae were clear, the ears and nose apparently normal. The teeth were in fair condition; small petechiae on both cheeks. Slight bleeding from the gums, tongue coated, pharynx slightly injected and the tonsils not enlarged. The thyroid and cervical glands were not enlarged. The chest was well developed; respiration equal but somewhat shallow. Small râles were heard over both bases. The breasts were negative. The left border of the heart measured 11 cm. to the left of the midsternal line in the fifth interspace. The sounds were somewhat distant but clear; there was a slight systolic murmur heard best over the apex and not transmitted. The pulse equal and regular; blood pressure 110 systolic, 60 diastolic. The examination of the abdomen was essentially negative. The extremities were negative except for slight edema in the lower and scattered purpuric eruptions. The vaginal examination disclosed a bloody discharge from the uterus, the cervix was rather firm and showed an old laceration, but no ulcerations. The cul de sac and fornix were negative. The fundus of the uterus could not be felt.

Fluoroscopic examination of the chest showed the lungs to be clear, the heart slightly enlarged in the lower transverse diameter, the diaphragm normal in position, the costo-phrenic angles clear. The urine was straw colored, clear, sp. gr. 1.008, alkaline, albumin 0.4% of 1%, no sugar; the sediment contained ten white cells per field, no red cells, no acid fast organisms, quite a few streptococci, no casts were found. Before the transfusion, the blood examination showed hemoglobin 45 per cent, the red cells numbered 2,170,000, the white cells 18,050 of which 85 per cent were polynuclears and 15 per cent small lymphocytes. The red cells showed marked variation in size and outline. No nucleated red cells were found at the first examination, subsequently a few were found but no reticulocytes. Four days after the first transfusion of 500 c.c. of citrated blood, 240,000 blood platelets per cumm. were found, the coagulation time was 3 minutes, and the bleeding time 5 minutes. The clot was not studied. The Wassermann reaction was negative. The sputum contained numerous fusiform bacilli, occasional spirochetae, a few streptococci and diplococci, but no acid fast organisms. Yeast cells were also present.

The treatment was of temporary benefit only. Following hypodermoclysis of salt solution, some fluids by mouth and transfusion of 500 c.c. of

blood, there was some improvement. The patient became more quiet, was able to talk rationally, and retained some food. Soon a swelling of the right parotid gland developed which yielded only a bloody secretion on incision. Her condition grew more serious, the restlessness and delirium returned with some stupor, severe hemorrhages from the rectum and vagina followed, and she failed to rally after a second transfusion. She died on March 20, 1929, just 13 days after admission to the hospital.

Autopsy performed soon after death by Dr. Joseph N. Ganim who was permitted to open the abdomen only. Protocol: Mrs. H. B., white woman, aged 37.

External Examination: The body is that of a middle aged, slightly obese, fairly well developed white woman measuring 166 cms. in length. The body surface is still warm and there is little apparent rigor mortis. The skin of the face is studded with a few discrete purplish pigmented areas covered with small crusts. Occurring rather infrequently on the thighs, arms and back are a few areas of pale, purplish ecchymoses. In addition the soft tissues of the right face along the angle of the mandible are swollen, somewhat indurated and of a purplish hue. A short wound one cm. in length is present just above this angle of the jaw on the right side. The body surface is otherwise negative except for a healed right rectus scar. Pelvic examination reveals a marital outlet, edematous cervical lips, an oval, smooth uterus but no palpable appendages.

Abdominal Cavity: The peritoneal cavity contains a few c.c. of pale, straw colored fluid. The omentum is adherent along the old right rectus scar. The abdominal viscera reveal little of note on external inspection. Except for an absent appendix, the gastroenteric tract is not remarkable. It contains no free blood.

Liver: The liver is normal in size. The capsule is smooth and the cut surface is pale, grayish-brown with fairly well preserved markings but increased friability. The gall bladder is not remarkable. The bile ducts are patent.

Spleen: The spleen is not enlarged. The capsule is shaggy, as the result of fibrous adhesions. The cut surface is pale brick-red and well preserved with equal prominence of the connective tissue markings and Malpighian bodies. Friability is slightly increased. The internal genitalia are not remarkable.

Kidneys: The adrenals are normal and well preserved. Both kidneys are infantile in size and nodular. The right measures 8.5 x 3 x 1½ cm. The respective weight of the kidneys is 43 and 48 gms. The nodular appearance is essentially in the parenchyma. This appears as cream colored, papillated tissue which in the cut surface closely resembles fat. The capsules strip with relative ease being only infrequently adherent. The cut surface is a combination of pink and gray hues. There is marked narrowing of the cortex and medulla. The markings are not recognizable. The ureters are patent and the urinary bladder, aside from being spacious is relatively normal.

Heart: The pericardium and heart, aside from some increase in size of left ventricle and some dilatation of the right side, reveals little additional

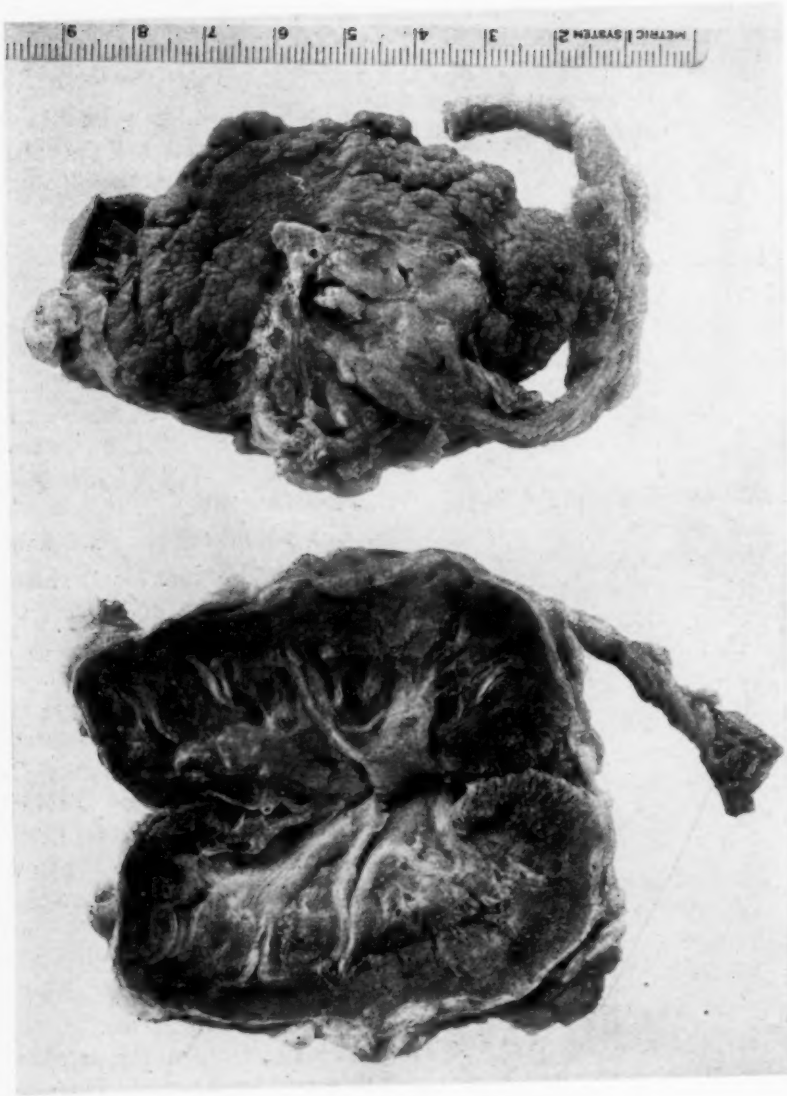


Fig. 1. Kidneys weighing 48 and 43 grams respectively; marked narrowing of the cortex and medula.

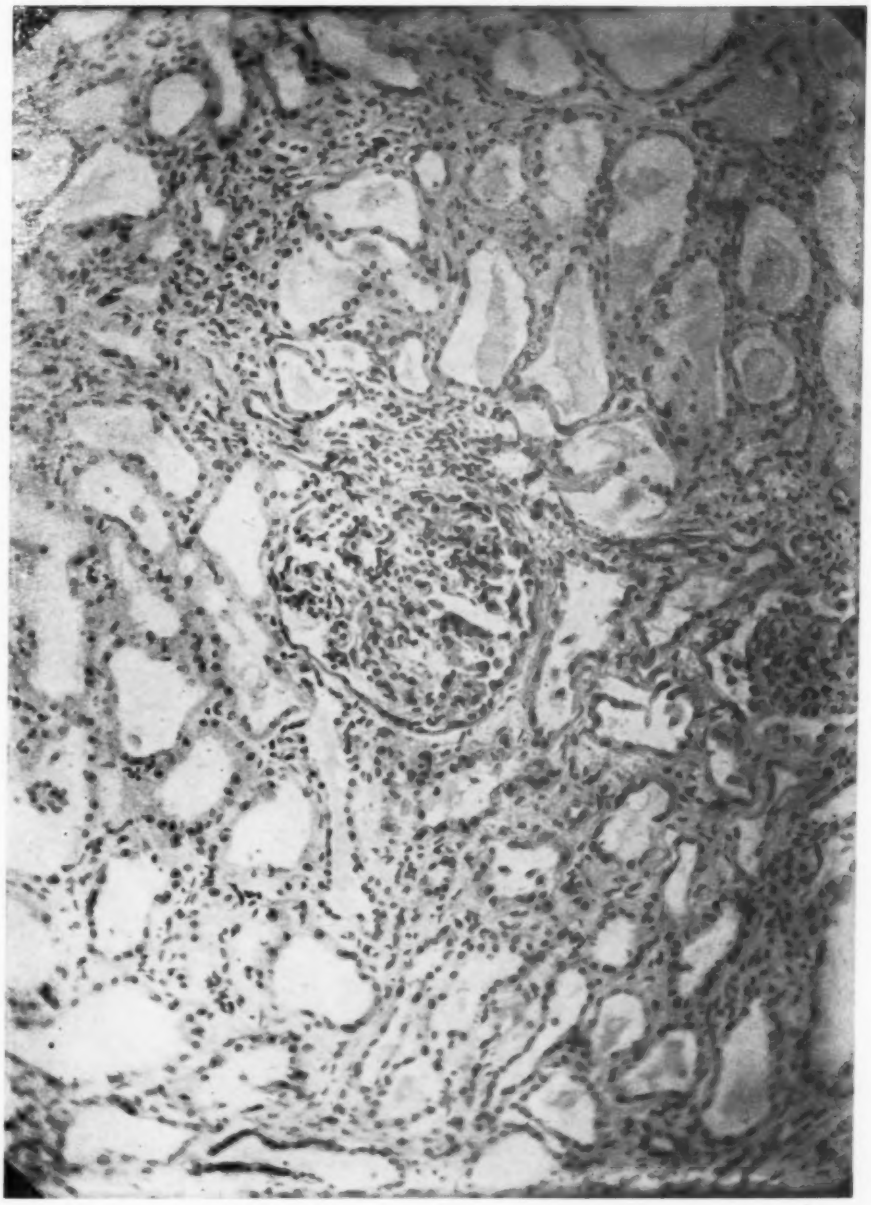


Fig. 2. Showing the dilated and distorted tubules; the sclerosis of the vessel walls; hypertrophy of the interstitial tissue; a large well preserved glomerulus with some sclerosis of the capsule. M x 200.

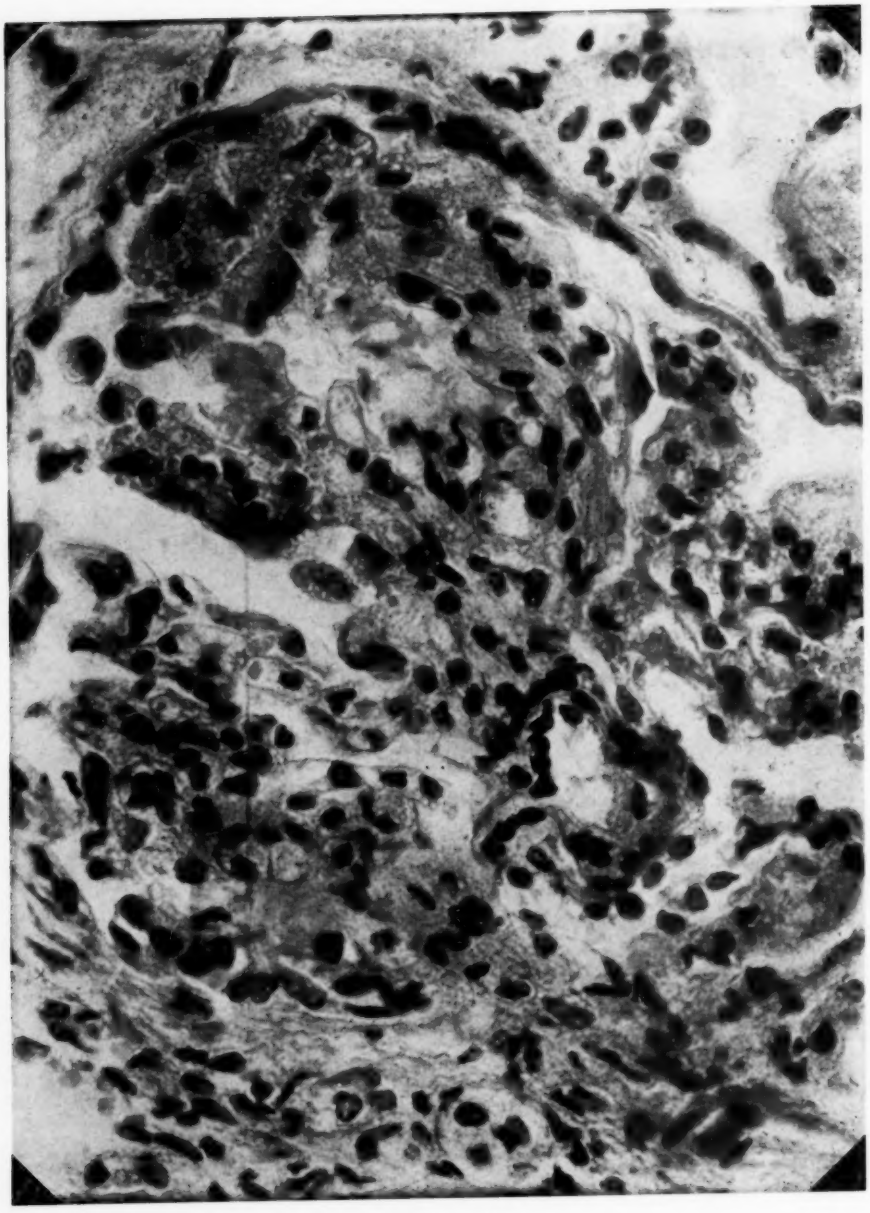


Fig. 3. The same glomerulus magnified 800 times.

pathologic changes. The coronary arteries and aorta are not remarkable.

Lungs: The right lung, especially the lower lobe and to a lesser extent the left lung, present numerous patches and confluent areas of small, moderately deep red pneumonic infiltrations varying from friable to relatively firm tissue. Only a few fibrous pleural adhesions are found on the right side. The tracheo-bronchial mucous membrane and corresponding lymph-nodes are not remarkable.

Microscopic Examination

Kidney: Renal capsule not present in section except for occasional small adherent thickened strip. Many glomeruli are sclerosed while others show thickening of capsule. The better preserved glomeruli show no appreciable increase or reduction of nuclei or tufts. The blood vessels especially the small show definite sclerosis most apparent in the intima. Most of the tubules are dilated and distorted; the lining epithelium is flattened and in some instances lay loose in the lumen. The lumina contain moderately pale pink hyalin-like bodies. The interstitial connective tissue is relatively increased and contains a goodly number of lymphocytes. The pelvis presents an intact mucous membrane and submucosa contains numerous lymphocytes and a few endothelial leucocytes.

Spleen: Capsule slightly thickened; lymphoid elements quantitatively reduced; framework is prominent; hyaline changes in thickened vessel walls.

Heart: Not remarkable.

Cervix: Dilated gland with epithelial hyperplasia of (glandular) cells; submucosa contains moderate number of lymphocytes.

Anatomical Diagnosis:

1. Chronic interstitial nephritis.
2. Active nontuberculous pyogenic lobular pneumonia.
3. Acute parotiditis.
4. Petechial hemorrhages and ecchymoses into skin.
5. Laparotomy scar.

Microscopic:

1. Chronic interstitial nephritis (contracted kidney).
2. Chronic fibrous splenitis.
3. Chronic cervicitis.

Summary

In a woman aged 37 death occurred as a result of simple symptomatic purpura and uremia; the autopsy disclosed the presence of markedly contracted kidneys weighing only 91 grams. The blood platelet count, the bleeding and clotting time were within normal limits. Renal complications had been present over a period of two years, but the purpuric symptoms had been either overlooked or manifested themselves only by increased menstrual flow, until a short time before her death.

References

[1]Little, E. G.: Cases of Purpura Ending Fatally, Associated with Hemorrhage into the Suprarenal Capsules, British Journal of Dermatology, Dec. 1901, Vol. XIII, pp. 445.

[2]Stevens, A. R.: and Peters, J. P., Jr.: Urinary Tract Purpura; A Probable Entity; Journal of Urology, Baltimore. Vol. IV, Feb., 1920, pp. 1-97.

[3]Nelson's Loose leaf Medicine, Vol. IV, Chapter III, pp. 128 and Chapter VI, pp. 159.

[4]Medical Times and Gazette, 1879, pp. 582.

[5]Duke, W. W.: Journal Exp. Med. 1911, Vol. XIV, pp. 265 and J. A. M. A. 1910, Vol. LV, pp. 1185.

A New Case of Syphilitic Tumor of the Stomach Cured by Antiluetic Treatment

By Max Einhorn, M.D., *New York*

THE older literature on syphilis of the stomach can be found in the papers of LeWald,[1] Eusterman,[2] and myself.[3]

A recent paper on syphilis of the stomach by Singer and Meyer[4] is of great interest in showing that cases of syphilis of the stomach most probably heal perfectly during life. The authors arrive at this conclusion from the following facts: In a period of six years these eminent surgeons found microscopic evidences of syphilis merely in four surgically resected parts of the stomach. During the same length of time not a single instance of gastric syphilis was encountered by them in five thousand autopsies. The authors assume that retrogression of the syphilitic infection in the stomach frequently occurs.

Whether this healing process takes place without any further medication or merely by the well known antiluetic remedies, is difficult to say. This, however, refers to the smaller lesions (ulcers, erosions, gastritis) but not to tumors of the stomach of a luetic nature.

The latter group appears but rarely, resembles real neoplasms so much, that it is usually taken for cancer, and is frequently accompanied by a fatal issue. This group is therefore of the greatest importance and I take pleasure in discussing this subject before you. In my practice I have seen altogether ten cases of syphilitic tumors of the stomach of which I have described seven in different papers.* Of the three more recent cases I shall report one, the last one observed. The case is as follows:

Herman S., 45 years old—Salesman. Sept. 25th, 1928.

Previous history: Never ill before, never operated upon.

Married 18 years, no children; wife was told she must be operated upon for sterility.

Patient denies venereal disease.

Present trouble started in March, 1928, with marked constipation. Appetite became poor. Bowels did not move in two or three days, whereas formerly they were always regular. Patient consulted his family physician who gave him some medicine and he felt better for three months. Then in May, 1928, patient complained of cramps in the legs and began ot feel dizzy. Appetite became poor again but improved after taking some medicine. Patient then felt good for one month. In June patient noticed that he was becoming pale and losing weight. He had X-ray pictures taken of his gastrointestinal tract and was told he must undergo an operation at once. He lost about

*Remark: 2, in my paper; Syphilis of the Stomach: Philad. Medical Journal, Feb. 3, 1900; 1, Journal of the American Medical Association, Oct. 25, 1902; 1, International Journal of Surgery, Jan., 1909; 3, Medical Record, March 13, 1915.

15-18 pounds from March until September 25, 1928, at which time he consulted me.

Chief complaints: Dizziness, loss of weight, weakness, loss of appetite, and pains in the legs. Patient looked pale and became exhausted on slight exertion.

Physical examination of the abdomen revealed a resistant mass of walnut size to the left of the median line but near it under the costal margin. The liver was slightly enlarged but not indurated.

The gastric contents examined one hour after Ewald Boas test breakfast showed: HCL=O; reaction hardly acid.

The gastric contents were again examined on Oct. 2nd with a similar result: HCL= trace; Acidity=10. The string test was negative. Wasserman++++.

A diagnosis of a probable syphilitic tumor of the stomach was made and patient put tentatively on an antisyphilitic treatment (Salvarsan and Iodides). Patient began to improve pretty soon after this régime. On Nov. 8th the resistance was still there but only a trace of it palpable. Patient felt stronger and reported a gain of eight pounds. On January 9, 1929, patient felt well and there was no resistance palpable in the gastric region. He continued to gain in strength and health. Beginning of February, 1929, patient showed a gain in weight of 30 pounds and his Wasserman became negative. It was of great interest to control the result of treatment with X-ray pictures taken at different times and to ascertain whether we could find a change in the anatomical state of the stomach. We give therefore the roentgenograms taken before and after treatment.

The interest this case presents lies in the fact,—that to all appearances patient seemed at first hand to be troubled with malignant neoplasm of the stomach. We had here a comparatively short history of disease, a palpable tumor, absence of hydrochloric acid in the gastric secretion, and a pronounced gastric defect by the X-rays. With all these pathognomonic signs there were present loss in weight and strength and severe dyspeptic symptoms. The presence of the Wasserman reaction (++++) gave a clue to the possibility of having to deal here with a gummatous tumor of the stomach. The course of the disease, its complete response to the instituted antiluetic treatment, and the disappearance of the Wasserman reaction after the cure, show that syphilis of the stomach was the only affection here present. This finds confirmation in the X-ray pictures which show a gradual recession of the tumor and return of the stomach to its normal configuration.

I take pleasure in thanking my associate Dr. H. A. Rafsky for the X-ray pictures and his assistance in the treatment of the case.

[1]Downes, W. A., and LeWald: Journal American Medical Association, May 29, 1915, page 1824.

[2]Eusterman: American Journal Medical Sciences, Jan. 1917.

[3]Einhorn, Max: Philad. Medical Journal, Feb. 3, 1900.

[4]Singer, H. A., and Meyer, K. A., Chicago: Syphilis of the Stomach; Incidence. Surgery, Gynecology, Obstetrics, Jan., 1929. 48:1-144.

FIG. 1. Roentgenogram of stomach of Herman S. on Sept. 19th, 1928 before treatment. A big defect is visible involving the antrum pylori and portion of stomach adjacent to it.

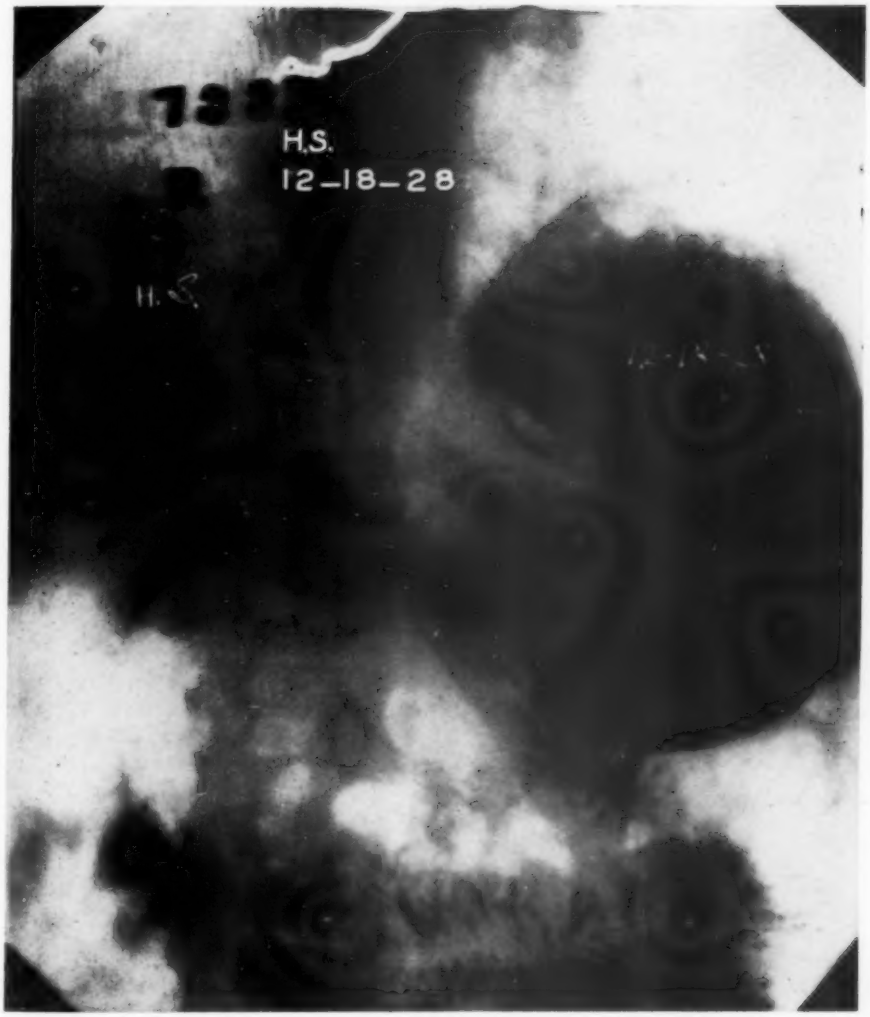


FIG. 2. Do. On December 18, 1928, or about two months after starting antiluetic treatment. The defect has decreased considerably.

FIG. 3. Do. February 1, 1929. The antrum and pars pylorica show up more favorably. The defect has almost disappeared.

The Treatment of Urticaria and Angioneurotic Edema*

By Grafton Tyler Brown, B.S., M.D., F.A.C.P., *Washington, D. C.*

URTICARIA and angioneurotic edema are commonly spoken of by the laity as hives and giant hives respectively. They are of frequent occurrence, and present to the physician one of his most difficult therapeutic problems.

This paper is based upon a careful study of a series of 160 patients with urticaria or angioneurotic edema. As the treatment of these two disease states is the same, I will deal with them together.

Allergic Relationship

Urticaria belongs to the group of allergic diseases which includes bronchial asthma, hay-fever, and eczema. There is a close relationship between urticaria or angioneurotic edema, bronchial asthma, and hay-fever, as evidenced by the following facts. In some persons, their asthmatic or hay-fever attacks are initiated or accompanied by urticaria. Some individuals with urticaria or angioneurotic edema have definite asthmatic symptoms with their urticarial attacks and at no other time, which seem to be due to edema within the bronchial tubes. For example:

One young woman with chronic urticaria, stated that she occasionally felt as if the hives broke out in her bronchial tubes, causing shortness of breath, and a wheezing sound which could be heard by others.

A woman with angioneurotic edema, stated that with her attacks of swelling, she had wheezing sounds in her chest.

Constitutional reactions from injections of extracts of foods, animal epidermals, pollens, etc., are frequently manifested by a combination of urticaria, angioneurotic edema, hay-fever, and asthma. Such constitutional reactions, as well as the urticaria of serum sickness, are best treated by epinephrine or ephedrine.

History Taking

The curative treatment of urticaria is, in most cases, based upon a specific diagnosis, and an exhaustive history is of fundamental importance in arriving at such a diagnosis. In other words, by careful questioning alone, the causative factors can frequently be elicited. The method of taking a complete history in urticaria is the same as in bronchial asthma, which has been fully dealt with in a preceding article.[1] I will give some illustrative excerpts from case histories.

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A boy of 10 years was brought to me with angioneurotic edema. His parents stated that when he was 6 years old, eating eggs caused his first attack, in which his ears were swollen, nose distorted, and all of his features changed. They also stated that eating certain kinds of nuts, especially English walnuts, affected his mouth, made his throat itch, and upset his stomach. Almonds and peanuts did not seem to bother him. Peanuts, of course, are not nuts at all, but belong to the legumes. After petting a dog, his hands would itch. On cutaneous tests, he gave an enormous reaction to English walnut protein, marked reactions to eggyolk ovovitellin and black walnut, and a moderate reaction to dog hair. Almond was negative, and peanut gave a slight or doubtful reaction.

A man of 50 with hives, stated that drinking grape juice caused them. He gave a marked positive reaction to a skin test with grape protein.

A 7 year old boy had hives within a few minutes, every time he ate eggs, and they were the only food that his parents had noticed would cause them. Out of 48 skin tests, his only positive reactions were to the different proteins of egg.

A young man of 18 said that eating buckwheat made him break out in bold hives. He gave a marked positive skin reaction to buckwheat protein.

A girl of 10 years was brought to me with urticaria. Her mother stated that milk disagreed with the child, and always caused red blotches around her mouth and generalized hives. She never used to vomit milk, but recently had been unable to retain it. On tests, the child reacted markedly to the protein of whole milk, and also to the casein and lactalbumin fractions.

A woman of 35 had angioneurotic edema. The attacks made her lips and tongue swell. There was an itching way in the back part of the roof of her mouth, and an itching deep in her ears, so that she felt as if she wanted to dig them out. There was also an itching and swelling in her throat, and her esophagus seemed tight. She gave as causes: bananas, tomatoes, celery, nuts, watermelon, grapes, figs, dates, and onions. All of the foods named gave positive reactions, with the exception of watermelon, figs, and dates, which were not tested.

A man, aged 31, had noticed for the preceding 9 years that eating cantaloupe or bananas would produce hives, and spinach would cause his tongue to break out in welts. A physician who would not believe that so healthful a food as spinach could harm anyone, gave him a hypodermic injection of the juice from cooked spinach, and it made him unconscious for two hours. He reacted to cutaneous tests with cantaloupe, banana, and spinach.

A woman, 32 years of age, stated that eating grapefruit caused severe urticaria, and cantaloupe made her throat itch. She gave a marked skin reaction to grapefruit protein, and a moderate reaction to cantaloupe.

People with urticaria are, of course, frequently suspicious of certain foods that have nothing whatever to do with their trouble. On the other hand, the failure to obtain a positive reaction to a skin test with the protein of some particular food is not sufficient to rule out that food as a cause.

Skin Tests

Positive reactions to skin tests are relatively infrequent in urticaria, in comparison with bronchial asthma. Someone has attempted to explain this discrepancy by stating that the urticarial reaction takes place in the blood vessels of the skin rather than in the skin cells.

As a positive reaction to a skin test is manifested by an urticarial wheal, one would think that skin tests would diagnose practically all cases of urticaria, but unfortunately they will not. For example, I have had two severe attacks of acute urticaria from eating too many tomatoes, and yet when I am tested with tomato protein that I know to be potent, I give absolutely no reaction to it. Therefore, when patients with urticaria are suspicious of certain foods that fail to give positive skin reactions, these foods should be completely eliminated from their diet for a sufficient length of time to prove their guilt or innocence.

Protein skin tests were made on 148 of the 160 patients with urticaria or angioneurotic edema in this series, and 60 per cent of those tested were found to be protein sensitive and 40 per cent negative. Sixty per cent sensitive, however, is too high a proportion for urticaria, as, in a number of the patients, the positive skin reactions were due to a concomitant asthma, hay-fever, or eczema.

False Reactions. In testing patients with irritable skin or dermographia, extreme care should be taken not to traumatize the skin any more than is absolutely necessary, and, to rule out false reactions, the tests should be interpreted in comparison with normal controls.

Doubtful Reactions. Even slight or doubtful reactions to skin tests are worthy of consideration, as evidenced by the following case reports:

A man of 51 consulted me in 1925, with urticarial attacks that he had been troubled with for the preceding 20 years. All of his skin tests were completely negative, with the exception of doubtful reactions to spinach and celery. These foods were eliminated from his diet, and he has been entirely free of urticaria ever since, a period of nearly four years.

A man, aged 55, was referred to me with angioneurotic edema of two years duration. The swelling always affected one side of his face and head. He gave slight reactions to the proteins of cows' milk. Milk was completely eliminated from his diet, and when last heard from, he was entirely well of his trouble.

In eliminating from the diet such foods as eggs, milk, or wheat flour, it is, of course, necessary to eliminate all other articles that contain them.

Delayed Reactions. Reactions to skin tests with food proteins almost always appear within five to thirty minutes. Occasionally, however, food reactions are delayed, and do not appear until some hours after the tests are applied. Therefore, if there are no immediate reactions, the sites of the tests should be examined at intervals during the succeeding 24 hours for the detection of delayed reactions.

Food Addition Method

Even though the history and skin tests are negative, a diagnosis may be made at times by means of the food addition method, originally advocated by O. H. Brown.[2] The patient is put

on an exclusive milk diet for about a week, and if the urticaria clears up, it proves the cause to be some food or foods other than milk. Other foods are then added to the diet, one at a time every few days, and the reappearance of the urticaria carefully watched for. In this way, the offending food or foods may be detected. If the urticaria does not clear up after about a week of an exclusive milk diet, a diet of all kinds of food except milk and milk products is substituted. If the urticaria disappears on such a diet, milk is proved to be the cause.

Non-food Sensitization

Although foods are by far the commonest cause, urticaria may also be due to sensitization to animal epidermals, bacteria, pollens, drugs, etc. I will cite a few cases.

A girl, 2½ years old, was brought to me with asthma and urticaria. The first attack occurred when her father put her on a horse. Her eyes got red, she began to wheeze, and broke out all over in hives. She reacted, of course, to a skin test with horse dander protein.

A woman of 32 was recently referred to me with bad urticaria of four or five years duration. It affected her face, neck, chest, back, and arms, and occurred at all seasons of the year. The urticarial eruption was accompanied by terrible itching, and would last anywhere from a few hours to a day, and then disappear, only to promptly recur. She had tried, without results, various diets and medicines that had been prescribed for her. Skin tests were all negative. Cultures of her stool showed streptococcus hemolyticus in large numbers, and an autogenous vaccine was prepared from this organism. When tested intradermally with the streptococcus hemolyticus vaccine, she gave a marked positive reaction. She was given injections of this vaccine at weekly intervals, in gradually increasing doses. Her urticaria promptly disappeared under treatment. It is interesting to note that following several of the increases in vaccine dosage, she had a transitory recurrence of the urticarial eruption.

A man was referred to me in 1924 with urticaria and dermatitis. He felt sure that his skin trouble was due to acid foods, and he named a long list of them that he could not eat. His attacks started the latter part of May and lasted throughout the summer. He had never had the least bit of this trouble in the winter. All food tests were completely negative, but he gave definite positive reactions to the pollens of the common grasses. In the spring of 1925, I gave him 16 rapidly increasing doses of grass pollen extract, and, in spite of eating whatever he pleased, he went through that summer without a sign of urticaria or dermatitis. I retested him in the spring of 1926, and he gave only very slight or doubtful reactions to the same grass pollens that he had been definitely sensitive to before treatment. He has had no treatment since, and there has been no recurrence of either urticaria or dermatitis.

A physician consulted me recently, with generalized urticaria that he had been troubled with almost constantly for the preceding seven months. As his urticaria began during the strawberry season, he thought at first that

they might be the cause, and had since been suspicious of eggs, wheat flour, and cheese. He had been under the care of a gastro-enterologist, and also a dermatologist, without results. On skin tests, he did not react to egg proteins, but did react to the proteins of wheat flour, strawberry, cheese, and a number of other foods. As he was using a dentrifice containing ipecac, I tested him cutaneously with powdered ipecac, and he gave one of his largest reactions to this substance. He was advised, of course, to eliminate from his diet all the foods to which he had reacted, and also to change his dentrifice. As a result, his urticaria cleared up. He had another acute attack of urticaria, however, after taking a small dose of cough medicine which he afterwards found contained ipecac.

Urticaria from ipecac sensitization is somewhat unusual. Peshkin,[3] and others[4] have called attention to the importance of ipecac sensitization as a cause of bronchial asthma in pharmacists, from inhalation of the drug in the preparation of Dover's powder. Peshkin also refers to urticaria of the hands and forearms from contact with emetin solution.

Quinine and acetyl-salicylic acid are the commonest drugs to cause urticaria. As Cooke[5] has already stated, drug sensitive individuals rarely give positive skin reactions to the offending drug.

Non-specific Factors

People with urticaria not infrequently state that their attacks are brought on or aggravated by one or more of the following: getting overheated, hot baths, nervousness, excitement, hurrying, alcoholic drinks, emotional strain, strenuous exercise, etc. These various influences all tend to cause an increased supply of blood to the skin, thus probably bringing more of the toxic substance to the skin capillaries. Patients should be advised to avoid, as far as possible, all such aggravating influences. Rough woolen clothing may be quite irritating, even to persons not sensitive to wool, and therefore should not be worn next to the skin.

Non-allergic Study

In addition to an exhaustive history and all necessary skin tests, the successful treatment of chronic urticaria and angioneurotic edema frequently depends upon a careful study of the patient as a whole. Such a study, in addition to a general physical examination, may include urinalyses, blood tests, determination of the basal metabolic rate, stool examination, bacteriological examinations, X-rays, etc. I will outline the general management of these cases, recommending somewhat didactically, those therapeutic measures that have seemed to give the best results.

Urinalysis. If the urine is too concentrated, namely if the specific gravity is too high, the patient should be advised to drink more water. If the urine is too strongly acid, the diet should be regulated to contain more of the alkaline foods, and less of the acid-forming ones. A teaspoonful of sodium bicarbonate in water, should be taken daily until the urine is alkaline. The litmus paper test is sufficiently accurate for determining the reaction of the fresh urine. The presence of albumin and casts indicates either a nephritis or a nephrosis, and calls for

further study, including a diligent search for some focal infection, and possibly a kidney function test, and blood chemistry. The detection of sugar in the urine calls for a blood sugar determination. A large amount of indican in the urine is strongly suggestive of intestinal putrefaction. Any tendency to constipation should be corrected by regulation of the diet, and administration of the simpler remedies, such as mineral oil, either plain or combined with agar-agar. Pus in the urine indicates infection somewhere in the urinary tract, and its source should be determined and properly treated.

Blood Examination. Red, white, and differential counts, and hemoglobin estimations, frequently give helpful information. A low red cell count, namely an oligocythemia, calls for arsenic, which may be conveniently administered in the form of liquor potassii arsenitis (Fowler's solution), starting with one drop in a little water, three times a day after meals, and increasing one drop daily until five or seven drops, then decreasing one drop a day until one, then stopping a week, and repeating. A decreased percentage of hemoglobin, namely an oligochromemia, calls for iron, which may be given in the form of subcutaneous injections of the green citrate, ¾ grain every three or four days; or iron may be given orally in 5 grain sugar-coated pills of ferrous carbonate, one or two pills to be taken three times a day after meals. In all cases of secondary anemia, a proper diet and generous doses of sunshine and fresh air should be prescribed. Leucocytosis and a relative increase of the polymorphonuclear neutrophiles is indicative of focal infection. A blood eosinophilia is suggestive, but not diagnostic of protein sensitization. The subject of eosinophilia in allergy has been dealt with in another article.[6]

Blood Calcium. The most valuable blood test that can be made in urticaria, is the determination of the ionic calcium. In a preceding paper on calcium deficiency,[7] the importance of standardizing the laboratory technic of calcium determination, and of establishing a definite calcium norm, has been emphasized. We have established for our laboratory technic 9.5 to 11 mgm. per 100 c.c., as normal calcium limits. Ten milligrams per 100 c.c. is average normal, and readings from 9.5 to 10 mgm. not inclusive, are considered low normal.

We found that 42 per cent of patients with bronchial asthma, 40 per cent of patients with eczema, 37 per cent of those with perennial hay-fever, and 28 per cent with seasonal hay-fever, had a definite calcium deficiency. Calcium determinations were done on 60 of the present series of 160 patients with urticaria or angioneurotic edema. Fifty-eight per cent had a definite calcium deficiency, and 23 per cent were low normal. Therefore, calcium deficiency is much more frequently encountered in urticaria and angioneurotic edema, than it is in asthma, eczema, or hay-fever.

Calcium Therapy. Patients with a low normal calcium should be given calcium lactate and parathyroid orally, and those with a definite calcium deficiency should be given the same, with the addition of air-cooled quartz lamp treatments.

According to the work of Roe and Kahn,[8] the optimum oral dose of calcium lactate is 5 grams, taken on an empty stomach. It has been found convenient to have the calcium lactate powder dispensed in a four-ounce glass jar, the screw cap of which level full holds 5 grams of the powder. The patient is instructed to pour a level capful of the powder on the surface of a glass of water, to wait until the powder all settles to the bottom of the glass, then to stir it up well and drink rapidly, following with a little clear water. This dose is to be taken twice daily, about one-half to one hour before breakfast and dinner, or the second dose may be taken at bedtime. Children are given 25 grains of the calcium lactate powder three times a day, one-half to one hour before meals. A half-ounce glass vial, the screw cap of which level full holds 25 grains of the powder, is supplied for measuring the doses.

For the occasional patient who cannot take the calcium lactate powder, 5 grain tablets of calcium lactate should be prescribed, one or two tablets to be taken three times a day, one-half to one hour before meals.

If it is desired to administer calcium intravenously, a sterile 10 per cent solution of calcium chloride should be used. The dose is from 2½ to 5 c.c., and may be given two or three times a week. The solution should be injected very slowly into the blood stream, and, as it is extremely irritating to the tissues, great care should be exercised to prevent any from escaping outside of the vein.

The dose of desiccated parathyroid is 1/10 grain for adults and 1/20 grain for children, prescribed in tablet form, to be taken three times a day, one-half to one hour before meals.

The mercury-vapor ultraviolet light treatments should be started with the quartz burner about 24 inches from the patient's body, for one or two minutes lying face down, and then for the same time lying face up. For subsequent treatments, the time should be increased by one or more minutes (depending upon the amount of skin reaction from the preceding treatment), until a duration of twenty to thirty minutes both back and front, forty to sixty minutes in all, is reached. Then holding the time constant, namely, twenty to thirty minutes each way, the lamp should be lowered 1½ to 3 inches at a treatment (depending upon reaction), until the burner is about 12 inches from the patient's body. In other words, the treatments should be so regulated that the patient will have a mild skin reaction following each exposure. These treatments should be given every 3 or 4 days. Amber goggles should be worn to protect the eyes. An interval timer should be used for timing the exposures.

Those patients who, for one reason or another, cannot take the ultraviolet light treatments, should be given cod liver oil in teaspoonful doses three times a day.

Other than calcium determination, additional blood chemistry, such as blood sugar or uric acid, should be done whenever there seems to be any indication.

Wassermann. Hazen[9] has mentioned syphilis as one of the causes of chronic urticaria. Wassermann and Kahn pre-

cipitin tests were done on 24 of my 160 patients with urticaria or angioneurotic edema, and they were all completely negative. It would seem that in urticaria, Wassermann or Kahn precipitin tests are indicated only where there is a history suggestive of lues, such as repeated miscarriages, frequent sore throat, etc.

Basal Metabolism. The basal metabolic rate should be determined on all patients who have symptoms of either hypo- or hyperthyroidism. For the metabolism test to be of any value, it is essential that the patient be basal at the time of the test. Rates from minus 10 to plus 15 are within normal limits. The basal metabolic rate was determined on 23 of the patients with urticaria or angioneurotic edema in this series, and of these, 8 were "hypo," 4 were "hyper," and 11 were normal.

Patients with a low metabolic rate should be given desiccated thyroid, which may be conveniently administered in tablet form. The dose is from 1/10 to 1 grain, three times a day, one-half to one hour before meals. It is preferable to start with 1/10 grain and then gradually increase the dose until the metabolism is brought to normal. The best single guide in thyroid dosage is the pulse rate.

Hyperthyroid patients should be instructed to take an abundance of rest, and all foci of infection, such as abscessed teeth or diseased tonsils, should be surgically removed. If the hyperthyroidism does not respond to rest and the removal of focal infection, X-ray treatment of the thyroid gland should be instituted.

One of the most intractable cases of chronic urticaria that I have seen, was that of a young woman with hyperthyroidism. Her basal metabolic rate was plus 33, and as she refused to rest, she was referred to a radiologist for X-ray treatment of the thyroid gland. After several treatments, her urticaria disappeared. When I last heard from her, however, she had discontinued her treatments, and there had been a recurrence of the urticaria.

Other Gland Therapy. Desiccated whole ovary or corpus luteum should be prescribed when there are symptoms of ovarian hypofunction, such as amenorrhea, irregular or scanty menstruation, or premature menopause (artificial or natural). The dose of either whole ovary or corpus luteum is five grains three times a day, one-half to one hour before meals. They may be conveniently administered in tablet form.

Desiccated whole suprarenal gland, one or two grains in tablet form, three times a day, one-half to one hour before meals, is worthy of trial in those patients with a definitely low blood pressure.

In urticaria due to food sensitization, pancreatin may prove helpful in promoting complete intestinal digestion of the various foods. Pancreatin should be prescribed in the form of 5 grain tablets with an enteric coating, so that they will pass through the stomach unchanged, as suggested by Sansum.[10] One or two of these tablets, usually the latter, should be taken after each meal.

Stool Examination. The stools should be carefully examined for the presence of parasites or ova, excessive putrefaction, or abnormal flora such

as streptococcus hemolyticus. Patients with excessive intestinal putrefaction or abnormal flora, should be given a saline, such as sodium phosphate, every morning upon arising, for about a week, to thoroughly clean out the intestinal tract. This should be followed by fresh acidophilus milk, one quart daily, in divided doses. Patients should be advised to add a teaspoonful of milk sugar (lactose) to each glass of the acidophilus milk. The eating of the dextrin-containing fruits, such as figs, dates, raisins, or prunes, should be encouraged as an aid to acidophilus therapy.

If fresh acidophilus milk cannot be conveniently obtained, buttermilk may be substituted. For those patients who cannot take large quantities of sour milk, one of the more concentrated acidophilus preparations may be prescribed, care being taken that it is fresh and viable, namely, contains large numbers of live bacilli.

Abnormal intestinal microorganisms, as for example the streptococcus hemolyticus, are usually swallowed from some focus in the nose or throat, such as infected sinuses or tonsils. The source of the intestinal infection should be eradicated as completely as possible. If the abnormal organism is present in the stools in considerable numbers, an autogenous vaccine should be prepared, and the patient treated with it.

Focal Infection. Foci of infection, any place in the body, should be removed as completely as possible. All abscessed teeth should be extracted. If no other cause can be found to account for the chronic urticaria or angioneurotic edema, all devitalized teeth should also be extracted, even though the X-ray shows no evidence of periapical bone destruction, as practically all pulpless teeth are infected.

Proper autogenous vaccine therapy is a valuable supplement to surgical or other treatment, in eradicating chronic infection. The preparation of autogenous vaccines, the selection of the proper organisms by means of intradermal vaccine tests, and the regulation of vaccine dosage, etc., have been dealt with in a preceding paper.[11]

Emergency Treatment

Isolated attacks of acute urticaria are usually due to some dietary indiscretion, and are best treated by the prompt administration of a purgative. In urticaria or angioneurotic edema, when the symptoms are at all severe, the emergency treatment par excellence is epinephrine hypodermically. From 8 to 16 minims (½ to 1 c.c.) of a 1 to 1000 solution of epinephrine should be injected, and repeated if necessary. Edema of the glottis may cause death. Therefore, in angioneurotic edema, when the edematous swelling seems to be affecting the throat or larynx, epinephrine should be administered without delay, and in sufficient dosage.

In chronic urticaria, epinephrine has certain disadvantages, in that it must be administered hypodermically to be effective, and the relief is of short duration.

Epinephrine solutions when fresh are colorless and clear like water. These solutions are relatively unstable, becoming readily oxidized upon exposure to the air, and are also affected unfavorably by exposure to light. Epinephrine solutions that have become darkened have lost considerable of their potency.

Symptomatic Treatment

The itching in urticaria, which is frequently intense, may be relieved somewhat by one or more of the following antipruritic remedies: cold baths, either plain or with soda; sponging the skin with alcohol, or a saturated solution of menthol in alcohol; calamine lotion containing one per cent phenol; ointments containing menthol or phenol. Ice compresses may be applied to the localized swellings of angioneurotic edema.

Bromides. Mixed bromides, 15 grains at a dose, should be prescribed, to be taken at bedtime when there is loss of sleep from itching, and two or three times a day when there is considerable nervousness.

Ephedrine. Ephedrine, the alkaloid of ma huang, which has been used in Chinese medicine for over 5000 years, is the most valuable oral drug that we possess, for the symptomatic relief of urticaria and other allergic conditions. Ephedrine hydrochloride is preferable to ephedrine sulphate, as it contains about 5 per cent more of the alkaloid. Some of the first ephedrine sulphate that was put on the market, contained a considerable amount of pseudo-ephedrine and was consequently relatively inert.

Although ephedrine is not as potent therapeutically as epinephrine, and is somewhat slower in its action, it nevertheless possesses certain distinct advantages over epinephrine; namely, it is effective when administered orally, its action is of much longer duration, and the solutions are quite stable upon exposure to air and light, and will even withstand boiling.

Ephedrine hydrochloride for oral administration may be prescribed in capsules, tablets, or in a 3 per cent aqueous solution. The adult dose is from ⅜ to ¾ grain (12 to 24 minims of the 3 per cent solution), the average dose being ½ grain (16 minims of the 3 per cent solution). The dose for children is from ¼ to ½ grain (8 to 16 minims of the 3 per cent solution), with an average dose of ⅜ grain (12 minims of the 3 per cent solution).

Non-specific Therapy

In urticaria, as in other allergic conditions, when the exact cause cannot be found and removed, some form of non-specific therapy should be resorted to. After having tried injections of sterilized whole milk, autogenous defibrinated blood, distilled water, horse serum, etc., I unhesitatingly recommend concentrated peptone solution, as it has given me by far the best results. I have found the commercial peptone solutions entirely unsatisfactory, probably because they are too weak. A sterile 33 1/3 per cent peptone solution should be prepared, after the method of Schiff,[12] containing equal parts of peptone siccum, glycerine, and water. Prior to treatment, the patient should be tested cutaneously with the peptone solution, as, if sensitization should exist, it would be extremely dangerous to inject the concentrated solution. The 33 1/3 per cent solution is given undiluted, the initial dose being one minim injected intradermally, the second dose two minims intradermally, the third dose three minims either intradermally or subcutaneously. For subsequent treatments the dose is usually increased by

one minim each time, depending upon the reaction in the individual case, until a maximum dose of sixteen minims (1.0 c.c.) is reached, then continued at this maximum dose. All doses larger than three minims, should be given subcutaneously. If it is preferred, the one and two minim intradermal doses may be omitted, and the treatments started with three minims subcutaneously. The peptone injections are given once or twice a week, usually the latter.

Desiccated peptone (peptone siccum) taken orally one-half to one hour before each meal, tends to temporarily desensitize against the various food proteins. It should be prescribed in capsules containing 7½ grains, one capsule to be taken one-half to one hour before each meal. Children are given 5 grain capsules, to be taken in the same way. Peptone is hygroscopic, namely takes up moisture from the air, and when it does, the powder contracts into a hard mass. In putting up peptone capsules, therefore, the capsules should be dusted inside and out with starch, and they should be dispensed in a tightly capped container.

Case Reports

Before closing, I will report briefly a few cases to illustrate some of the phases of treatment referred to.

A young woman was sent to me in May, 1925 with severe angioneurotic edema, which had started eight months before, following the extraction of an abscessed tooth. At various intervals since then, four other abscessed teeth had also been extracted. Her trouble started with swelling of the fingers, and then affected the toes and heels. The joints got red and swollen, and were very painful. The swelling would stay a day or two in one joint and then jump to another. Her elbows and larger joints were not involved until later, and they were not as badly swollen. Two or three weeks after the trouble started, her lips became swollen, and the swelling gradually spread to other parts of her face. At times her eyelids were swollen shut. The swellings stung, and were very sensitive. Her body finally became practically covered with hives of various sizes, which lasted about 10 days. Although she still had them on her body, the swellings had recently involved principally her eyes and mouth. Her arms, legs, and body itched a great deal. At one time she had a very large swelling in her throat, which was relieved by an injection of epinephrine. I also found it necessary to administer epinephrine on three different occasions for the relief of marked swelling about her mouth. She had not been entirely free of urticaria or angioneurotic edema at any time during the preceding eight months. She thought that exertion, especially to the point of fatigue, aggravated her trouble. She also stated that eating chocolate made her break out in pimples. Her skin tests were all negative with the exception of a delayed positive reaction to chocolate and a positive reaction to orris root. She was advised to eliminate chocolate from her diet, and to avoid the use of face or body powders, etc., containing orris root. Her hemoglobin was only 76 per cent (Dare), for which she was given injections of iron. Cultures from the roots and sockets of the last two teeth extracted showed streptococcus hemolyticus and streptococcus viridans. When tested intradermally with autogenous vaccines of these organisms, she gave enormous reactions. The reaction to streptococcus hemolyticus was 4 inches in diameter, and viridans was 2 inches across. She was treated with these vaccines in gradually increasing doses, and the angioneurotic edema and urticaria disappeared. Her treatments were discontinued over three years ago, and she has had no recurrence of the angioneurotic edema, although she has an occasional small hive.

A woman, 27 years of age, consulted me in November, 1925 with angioneurotic ede-

ma, which she had been troubled with practically all of her life. Formerly, these attacks had occurred only in the spring, but in the preceding 6 or 7 years, they had occurred at all seasons. Each attack would usually last for 3 or 4 weeks. She would break out in great red blotches larger than the palm of her hand. The attacks often affected her eyelids, causing them to swell shut. There was no particular food that seemed to disagree with her, and she did not know of anything that would bring on an attack. She had tried various diets, etc., for the condition, but nothing seemed to help. Even injections of epinephrine failed to give complete temporary relief. She was gaining in weight, and had a subnormal temperature and a slow pulse. Her skin tests were all negative, with the exception of a few slight or doubtful reactions to substances which did not seem to have any bearing on her trouble. Her blood calcium was unusually low, namely 7.7 mgm. per 100 c.c., and her basal metabolic rate was minus 19. She was, therefore, given calcium, parathyroid, and thyroid orally, and ultraviolet light treatments. As a result she has had no further attacks.

A woman 43 years old was referred to me with angioneurotic edema, affecting principally her lips. The trouble had started about 6 years before, with attacks of swelling about the eyes, and an urticarial rash on the neck and various parts of the body. She had had a great many of these attacks at varying intervals; but in the preceding year, they had occurred much more frequently, and her lips had become affected. The attacks came on quite suddenly. The first symptoms noted were itching and burning of her lips. Then the lips would swell for several hours, until they were two or three times their natural size. They then looked as if they were filled with water, similar to a large blister. This swelling was accompanied with a feeling of tightness, and at times intense pain. After a certain amount of swelling, the lips would break open and discharge a sticky fluid which would dry and form crusts. When the lips would break, the tightness would be relieved, but they were very sore afterwards. Each attack would last about a week, and they had a terrible effect on her nervous system. She thought that the trouble was due to eating sea food. She had been in the hands of a number of competent physicians, without results. Cutaneous and intracutaneous tests for protein sensitization were all completely negative. She had one devitalized tooth (upper left first molar) but there was no radiographic evidence of pathology. Her blood calcium was 9.2 mgm. per 100 c.c. The devitalized tooth was extracted, and cultures from the roots and socket showed staphylococcus pyogenes aureus in pure culture. Calcium and parathyroid were prescribed, and she was given ultraviolet light treatments, and injections of an autogenous vaccine prepared from the tooth cultures. She was discharged well, over a year ago, and has had no sign of trouble since.

A woman 41 years of age, was referred to me in August, 1927, with angioneurotic edema of six months duration. Although practically all parts of her body had been affected, the tissues around her eyes bore the brunt of the attacks. For temporary relief, she was given hypodermics of epinephrine, followed by ephedrine orally. Skin tests were all negative. Her red cell count was 4,070,000 per cubic millimeter, and her hemoglobin was 76 per cent (Dare). Her blood calcium was 9.7 (low normal). Calcium lactate, parathyroid, and solution of potassium arsenite were prescribed, and she was given injections of green citrate of iron. She was discharged entirely well, and when last heard from, there had been no recurrence of the angioneurotic edema.

A girl of 6 years was brought to me in January, 1928. She had been bothered with hives off and on since she was 14 months old. Her parents stated that her first attack of urticaria followed eating egg, and that she had not been able to eat eggs since, as they would break her out in hives in about ten minutes. The hives were usually worse around her mouth. Skin tests with the proteins of egg were completely negative. She gave instead a marked positive reaction to cottonseed protein. Eggs were returned to her diet, and all cottonseed oil products

(substitutes for olive oil and lard) were eliminated. Since then she has been entirely free of urticaria.

A woman 52 years old was referred to me with urticaria which she had been troubled with off and on since childhood. She stated that she was constipated and had a great deal of gas. She had chronic nasopharyngitis, and the discharge from her nose was yellowish in color. Her skin and hair were abnormally dry, and she had a subnormal temperature and a slow pulse. Her urine was of high specific gravity, very strongly acid, and contained a large amount of indican. Her basal metabolic rate was minus 11, and her blood calcium was 9.4 mgm. Cultures from her nasal secretion and throat showed staphylococcus aureus and streptococcus hemolyticus, and cultures from her stool also showed streptococcus hemolyticus. She gave marked positive reactions to intradermal tests with autogenous vaccines of these two organisms. She was advised to drink more water, and eat more of the alkaline foods, and less of the acid-forming ones. Calcium, parathyroid, and thyroid were prescribed. Acidophilus milk was also advised. She was given injections of the aureus and hemolyticus vaccines at weekly intervals, in gradually increasing doses. As a result she has had no more urticaria.

Summary

Urticaria and angioneurotic edema are of frequent occurrence, and present to the physician one of his most difficult therapeutic problems.

In this paper, based upon a careful study of 160 patients with urticaria or angioneurotic edema, a comprehensive method of treatment is described, and illustrated with excerpts from case histories.

REFERENCES

[1]Brown, G. T.: History Taking in Bronchial Asthma. J. A. M. A. 88:1693 (May 28) 1927.

[2]Brown, O. H.: Protein Desensitization and the "Food Addition Method" in Asthma. Southwestern Med. 6, No. 8 (Aug.) 1922.

[3]Peshkin, M. M.: Ipecac Sensitization and Bronchial Asthma; J. A. M. A. 75: 1133 (Oct. 23) 1920. Bronchial Asthma and Other Allergic Manifestations in Pharmacists; ibid. 82:1854 (June 7) 1924.

[4]Widal, F., Abrami, P., and Joltrain, E.: Anaphylaxis to Ipecac. Presse med. 30: 341 (April 22) 1922.

[5]Cooke, R. A.: Allergy in Drug Idiosyncrasy. J. A. M. A. 73:759 (Sept. 6) 1919.

[6]Brown, G. T.: Eosinophilia in Asthma, Hay Fever and Allied Conditions. J. Lab. & Clin. Med. 12:1145 (Sept.) 1927.

[7]Brown, G. T., and Hunter, O. B.: Calcium Deficiency in Asthma, Hay-Fever and Allied Conditions. Ann. Clin. Med. 4:299 (Oct.) 1925.

[8]Kahn, B. S., and Roe, J. H.: Calcium Absorption from the Intestinal Tract in Human Subjects. J. A. M. A. 86:1761 (June 5) 1926.

Roe, J. H., and Kahn, B. S.: Absorption of Calcium from the Intestinal Tract of Human Subjects. J. A. M. A. 88:980 (March 26) 1927.

[9]Hazen, H. H.: Diseases of the Skin. St. Louis, C. V. Mosby Company, 1915, p. 340.

[10]Sansum, W. D.: The Normal Diet. Ed. 2, St. Louis, C. V. Mosby Company, 1927.

[11]Brown, G. T.: Bacterial Vaccines in Asthma. Am. J. M. Sc. 171:94 (Jan.) 1926.

[12]Schiff, N. S.: Non-Specific Versus Specific Therapy in Bronchial Asthma. Am. J. M. Sc. 166:664 (Nov.) 1923.

The problems Pertaining to the Proper Management of Allergic Phenomena, with Special Reference to Non-Specific Therapy in Bronchial Asthma and Hay Fever. Ann. Clin. Med. 5:374 (Oct.) 1926.

Obesity

Procedure, Classification, Treatment, And Results, In 151 Cases Studied During The Past Six Years, With Special Reference to An Endocrinopathic Origin.*

By Joseph Eidelsberg, M.D., *New York*

MUCH has been written on the subject of Obesity, and the literature on the study of the condition is certainly voluminous. However, there still remains a vast amount to be uncovered, and explained. Recently there have appeared several expressions of doubt as to an endocrinogenic factory in obesity,[1,2] and placing its incidence below one per cent. No "normal healthy adult" measures his food intake in grams of carbohydrate, fat and protein, and then, to keep his weight stationary, proceeds to work and exercise, play and rest in a measured caloric-equivalent amount. Still, some will gain weight, while others on the comparatively same, or identical schedule will lose weight. This truth, so well known to all, layman and scientist, is proof enough that even in many so-called simple exogenous obese, there must be other underlying disturbances—metabolic and endocrine.[3,4] Therefore, an analysis of the study and treatment of 151 cases during the past six years, helps to cast some light on the effects of treatment, and on the consideration of etiology.

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Definition

No case was considered obesity, unless the weight, for the sex, age, height, and configuration, was at least 20% greater than the standards given as normal.

Procedure

Having thus admitted a patient as "obese," a routine procedure was instituted:

1. History, with special reference to family history of Endocrinopathies and Obesity; personal history pointing to endocrine disease and weight curve, menstrual, marital, and sex history, appetite and food intake, exercise, etc.
2. Physical Examination, with special reference to endocrine signs, fat distribution, hair, teeth, skin, sex organs, measurements, etc.
3. Laboratory examinations, especially, X-Ray of sella turcica, sugar tolerance, X-Ray of thymus, basal metabolism, and blood chemistry.
4. Each patient brought us his or her food consumption over a period of 5 days (without change from previous routine), and daily work and exercise chart.

Classification

With this data before us, each case was placed into its proper category in the following classification:

1. *Exogenous*—where no abnormal findings (physical or laboratory) were revealed, and where the food intake was sufficiently high, in proportion to the work and exercise, to warrant considering a positive caloric balance.

2. *Endocrinopathic*
   (a) Pituitary disease—as evidenced by girdle obesity, small sella turcica, delayed menses or amenorrhea, deficient sex organs, increased sugar tolerance, etc.
   (b) Thyroid disease—present or absent struma, low basal metabolism, slow pulse, myxedematous infiltration, etc.
   (c) Thymic origin—type, low blood pressure, deficient sex apparatus, positive Thymic X-Ray, etc.
   (d) Pre-diabetic type—as shown by marked sugar tolerance decrease.
   (e) Gonadal type — trochanteric obesity, castration, menopause, etc.
   (f) Mixed types — pluriglandular disease.

3. *Idiopathic or Constitutional*[5]—a group of unexplained obese,—not exogenous, and not affected by any or all types of treatment.

The 151 cases were divided as follows:

81—Exogenous
46—Endocrinopathic.
20—Idiopathic or constitutional.
3—Lipomatoses, Lipodystrophy, etc.
1—Dercum's Disease.

The 46 Endocrinopathic cases were redistributed as follows:

Pituitary	28
Thyroid	10
Thymic	2
Pre-Diabetic	2
Gonadal	2
Mixed	2

Treatment and Results

The exogenous cases were placed on a diet as follows:

"Take only half of the quantity of each food that you are accustomed to take! Use no desserts that are prepared with flour or sugar! Take at least one fresh fruit and vegetable three times a day! The following articles of diet are recommended because of their low fat and carbohydrate (sugar and starch) content—these two elements of food being the principal fat producing and fat saving agents of food.[6]

"Animal Foods"—To be baked, broiled or boiled except where indicated otherwise. Lean chuck, loin and round steak; lean ribs of beef, all ground or cooked whole; lean leg of shoulder, loin and roast or veal. Lean chicken and other fowl, except goose, turkey, duck or squab. All fresh fish except butterfish, salt water eel, salmon and shad. May take clams, crabs, lobsters. No pork in any form to be taken.

"Dairy Products" — Buttermilk, skimmed milk, cottage cheese (the only variety of cheese allowed) eggs in any form allowed, except fried. No butter!

"Pickles, Condiments" — Tomato catsup, horseradish, vinegar, sour cucumbers, pickles, cabbage and cole

slaw. Pepper not allowed. Salt used sparingly.

"Fresh Fruit"—All fresh fruits may be used in moderation. Any fruit may be cooked in any form if sugar is not used in their preparation.

"Nuts"—All nuts are fat except chestnuts and are not to be eaten. Not over six (6) chestnuts should be eaten in one day.

"Fresh Vegetables"—The following may be used—Asparagus, celery, brussels sprouts, lettuce, cucumbers, endive, spinach, rhubarb, sauerkraut, cauliflower, egg plant, green peppers, kohl-rabi, leeks, radishes, string beans, cabbage, okra, turnips, and onions.

"Bread"—No bread may be used.

"Cereals"—Not over a tablespoonful of any breakfast food after it is cooked, with equal amount of Kellogg's bran mixed with it. If milk and sweetening are required, use skimmed milk and sugar substitutes.

"Drinks"—No beers, wine, nor heavy liquors. Black coffee or tea once a day. Use skimmed milk, butter milk, and no sweet soda fountain drinks may be taken.

The change in weight at the end of six months varied from a gain of 2 lbs. to a loss of 70 lbs., average 44 lbs. lost. In some cases (17) thyroid was added in doses varying from ½ grain to 5 grains (daily)—and a definite increase in loss of weight was observed. The pulse rate was not permitted to get above 90, (taken after reclining 20 minutes)—and any symptom or sign of excessive thyroid medication called for a rest of 5 to 10 days. Not one example of ill effects was observed. We firmly believe that though a certain degree of danger exists in the use of thyroid substance, it is minimal, or nil, when the patient is well controlled and observed.[7]

The endocrinopathic group received the diet and exercise treatment, plus organo-therapy, as indicated. On diet and exercise alone this group lost 2.1 lbs. average, per person, during a trial period of 6 weeks. Our largest group, the pituitary group, received pituitary substance by mouth in doses from 10 to 30 grains daily, with posterior pituitary solution by injection, varying from ½ c.c. twice weekly to 1 c.c. daily. The addition of thyroid gland by mouth aided the reduction materially, although some definite loss occurred usually without it. The loss of weight in 6 months in this group varied from 3 lbs. to 92 lbs. average per person for 6 weeks, 13 lbs.

The idiopathic or constitutional group failed to respond to any type of treatment, or diet restriction, including low caloric diet, salt free diet, water restriction, etc. This group impressed us as a type of pluriglandular disease, with some missing incretion, but on the whole they cannot take thyroid substance without symptoms.

B. M. R. Observations

An observation of note was made in 22 cases, where the B. M. R. was found increased, between 12% and 34%, unexplained by any previous drug therapy or gland therapy. We disregarded this in our treatment. This observation has been made by others[8,9] and the explanation is as yet purely theoretical.

SUMMARY

The classification of 151 cases studied during the past six years is given.

The method of classifying and treatment is outlined.

The results are briefly stated.

Increased B. M. R. were observed in about 15% of all the cases studied.

CONCLUSIONS

Obesity, regardless of type, can in a large measure be reduced,—excepting a group, which for want of a better term, is as yet labelled Idiopathic or Constitutional. Diet alone—reduction in caloric intake to below caloric expenditure—cannot affect all obese to produce weight reduction. Endogenous obesity is not a myth, nor a misconception, while exogenous obesity has often an endogenic or endocrinous etiological factor. Finally, we think, that if we group together all the cases of obesity, we will have at one extreme, the purely exogenous obesity, and at the other extreme, the purely endogenous obesity, of various types, but between these extremities the greatest group of mixed cases, all with a metabolic defect,—and here and there a so-called idiopathic or constitutional case. In treatment, all these things must be borne in mind. The problem is too complex, to be treated by so simple a formula as mere diet reduction, but instead we must add organo-therapy and other measures, as indicated.

REFERENCES

[1]EVANS, FRANK A., and STRONG, JAMES M.: A Departure From the Usual Methods in Treating Obesity. Am. J. of Med. Sc., March, 1929.

[2]BAUMAN, LOUIS: Obesity—Recent Reports in the Literature and Results of Treatment. J. A. M. A., Jan. 7, 1928, Vol. p. 22.

[3]GRAFE, E., and GRAHAM: Ueber die Aupassungsfähighkeit des Tierischen Organismus an uberreichliche Nahrungazufuhr. Ztsch. F. Physial. Chem. 73:, 1911.

[4]STROUSE, SOLOMON, and DYE, M.: Relation Between Food Intake and Body Weight in Some Obese Persons. Arch. Int. Med., Sept., 1924, p. 267.

[5]VON NOORDEN, C.: Ueber die Verschiedenen Formen der Fettsucht. Med. Klin. 5:, 1909.

[6]HAGEDORN, et al.: Metabolism in Obesity. Arch. Int. Med., July, 1927, p. 37.

[7]JOHN, H. J.: Treatment of Obesity with Special Reference to Dangers in Use of Thyroid. Med. J. and Rec., Oct. 19, 1927, p. 476.

[8]STROUSE, S., et al.: Studies on Metabolism of Obesity. Arch. Int., Med., Sept., 1924, p. 275.

[9]HAUSSLEITER, H.: Ueber den Gas. verschiednen Formen von Fettsucht und seine Beeinflussung durch Nahrings-arbeit und Arzneimittel. Ztschr. f. exper. Path. u. Therap. 17:413. 1915.

A Case of Pregnancy Complicated by Cardiac Decompensation and Anemia Gravidarum

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DURING the past few years the attention of both obstetricians and internists has been actively engaged by the problem of cardiac disease in pregnant women. Some interest has developed also in that curious type of essential anemia which is occasionally associated with the pregnant state. It seems worth while, therefore, to record a case which presented both of these complications, each in a severe form.

Report of Case

Mrs. C. B., an Italian housewife of 36, entered the Waltham Hospital on February 1, 1928, early in the eighth month of her fourth pregnancy.

The only significant item in her past history was rheumatic fever, of which there had been two attacks, ten years and one year previously. The obstetrical history of the first three pregnancies was uneventful.

The present illness began two months before admission, with cough, dyspnea, and malaise. The patient was treated by another physician for bronchitis, but all her symptoms grew steadily worse. The cough became constant, with profuse expectoration; dyspnea and prostration increased; and she began to have gastric distress after eating, frequently vomiting undigested food.

Examination revealed first of all a marked pallor. The heart was enlarged to the left, to the right, and downward, and a soft blowing systolic murmur was heard over the whole precordium. The lungs showed no dulness, but scattered râles were audible on both sides. The uterus was enlarged to the size of a seven months' pregnancy, the fetus lying in the right sacroanterior position. On vaginal examination the introitus was found to be roomy; the cervix was long and hard. Pelvimetry gave normal bony measurements.

On admission the red blood count was 2,500,000 and the hemoglobin 55 per cent; the stained smear showed nothing definitely abnormal except achromia. The urine was essentially negative. Four examinations of sputum failed to reveal tubercle bacilli. X-ray of the lungs showed increased lung-markings on the right, and small areas of increased density on both sides.

After careful consideration, we decided to institute treatment for the cardiac condition and the anemia, and, in event of definite improvement, to allow the pregnancy to continue either to term, or at least until such time as the baby's chances would be better.

The cardiac decompensation was treated by rest, sedatives, and different preparations of digitalis. Glucose also was given both by rectum and in small amounts intravenously. For the anemia the patient received, in addition to suitable diet, injections of liver extract. Transfusion was considered and rejected, mainly because of the extra load which a sudden increase in the blood-volume would throw upon an already laboring heart.

In spite of these measures the hoped-for improvement did not manifest itself. The cardiac condition remained the same; dyspnea and cough were exhausting the patient's strength, and the congested stomach

was retaining only a small part of the food taken. The anemia, on the other hand, grew more and more severe; on February 19 the red count was 2,040,000 and the hemoglobin was reduced to 35 per cent. Thus it became obvious that the mother's life would surely be sacrificed if the pregnacy were allowed to continue further.

On February 22 the patient was delivered by caesarean section, under scopolamine-morphine and local novocaine anaesthesia. Sterilization was done by the Madlener method. The operation was remarkable chiefly for the exceedingly small amount of blood lost. The child, a healthy male weighing six pounds, showed no evidence of prematurity, and did well from the start.

For the first week the convalescence was stormy. All the previous symptoms persisted, requiring a careful balancing of sedative and stimulant treatment. Extreme restlessness and some air-hunger developed. On February 25 a transfusion of 600 c.c. of blood was done by Dr. H. Quimby Gallupe. For several days thereafter frequent inhalations of oxygen were given.

On the second week the gastric congestion subsided, and the patient became able to take and retain a normal diet. The third week was marked by a diminution in the cough. From that time on the cardiac condition improved steadily, until compensation was fully established.

The improvement in the blood was striking. On March 4 the red blood count was 3,600,000 and the hemoglobin 50 per cent. On April 9 the red count had risen to 4,500,000 and the hemoglobin to 65 per cent.

The incision failed to heal by primary union, as not uncommonly happens with profoundly anemic tissues. Nevertheless a sound scar was ultimately obtained.

Now, a year after delivery, the patient considers herself to be in good health. She is able to lead a normal life and to perform her domestic duties without any obvious incapacity.

Discussion of Case

This patient presented the most serious cardiac complication of pregnancy—broken compensation which fails to improve under treatment. If she had been seen earlier, abortion would have been imperative. If she had reached full term, the question would have arisen whether she might be delivered with less risk by caesarean section or by a forceps-operation eliminating the second stage of labor. As the situation actually was, we felt that immediate delivery was indicated, and that caesarean section was safer than the double procedure of induction of labor and delivery from below. The opportunity to do sterilization was undoubtedly advantageous, but did not influence us to choose abdominal delivery. Regarding anesthesia, in our opinion ether was absolutely contraindicated by the pulmonary condition, though it might have been tolerated by the heart.

The anemia in this case was of the type that has been called puerperal anemia, or chronic hemolytic anemia due to pregnancy. The second name is cumbersome; the first is not strictly accurate, since the disease may develop in the late months of pregnancy (as in our present case), as well as during the puerperal state. Hence we prefer the more general term anemia gravidarum.

This condition must not be confused with pernicious anemia. Gallupe and O'Hara[1] say: "Pernicious anemia is the name of a definite disease syndrome, and should not be used as a descriptive name for any profoundly anemic condition. Puer-

[1]Gallupe, H. Quimby, and O'Hara, Dwight: Puerperal Anaemia. Boston Medical and Surgical Journal, Vol. 190, No. 5, pp. 161-164, Jan. 31, 1924.

peral anemia is an entity in itself, and should not be called pernicious anemia associated with pregnancy." It should be distinguished also from the anemia consequent upon hemorrhage and from that due to sepsis.

True anemia gravidarum is a grave condition, which in spite of all medical treatment becomes progressively more severe and terminates fatally in a majority of cases. Transfusion is a life-saving measure; it produces an immediate improvement and usually tides the patient over until complete recovery is established.

This case emphasizes again the need for the closest coöperation between the obstetrician and internist in handling the serious medical complications of pregnancy.

Undulant Fever

Report of Five Cases

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JUDGING from the medical literature of the past two years it seems that I am one of the few remaining physicians in the United States who has not reported one or more cases of undulant fever. I therefore hasten to add my quota.

No attempt is made to review the literature or to discuss anything of the distribution, etiology or bacteriology of this disease as these features are necessarily fresh in the minds of every one.

Two of these cases perhaps have points of interest in that one of them was not affected in any way by the intravenous use of mercurochrome (some writers have reported immediate cures following such treatment) and another seemed to show no encouraging results from the use of a one (1) per cent solution of tartar emetic intravenously.

The five cases were seen at the Station Hospital, Fort Sam Houston, Texas, during the years 1924, 1925, and 1926. Unfortunately no absorption agglutination tests to differentiate B. melitensis and B. abortus were made in these cases, although the procedure was carried out later in other cases, notes on which are not available at this time. Also all the blood cultures were negative for B. melitensis. Thus the diagnosis in each case is based almost entirely on the elimination of other diseases and the positive agglutination tests for B. melitensis, although in Cases I and II the history and the clinical course are quite typical.

The case histories are reported as briefly as possible.

Case I

B. N. C., white, male. Age thirty-two years. Admitted September 7, 1924. Family history: Unimportant. Previous personal history: Hookworm at fourteen or fifteen years of age. Malaria in 1916. Amebic dysentery, 1916. Gonorrhea in 1920. Had spent a great deal of time in Mexico for the previous three years, where he used, frequently, goats' milk and cheese made from goats' milk.

Two weeks before admission to hospital he was sick at Laredo, Texas, with "Intestinal fever." Had headache and pain in various regions of body. On admission to hospital felt weak but had no particular complaints.

Physical examination: Nothing remarkable.

Briefly, the patient went through a four and one-half months' course of undulant fever, apparently unaffected by any treatment. The graphic temperature chart shows the duration of the exacerbations and remissions to be as follows: Exacerbation seventeen (17) days. (Temperature up to 104.4° F., lysis); remission five days; ex-

acerbation twenty-four (24) days (temperature up to 105.2° F., lysis); remission three days; exacerbation thirteen days (temperature up to 101.8° F., lysis); remission three days; exacerbation seven days (temperature to 99.6° F.); remission six days; exacerbations for one or two days at irregular periods, temperature going from 99 plus to 100, for forty-three days, then an exacerbation for eight days (temperature up to 102.6° F., lysis).

There were occasional slight P. M. elevations of temperature for three months after the last fever curve and the symptoms of weakness, joint pain, and constipation were present more or less over most of this period. No enlargement of the spleen was noted at any time.

The urine was negative except that, during the temperature rises, albumin and hyaline casts were present frequently. Urine cultures negative for typhoid. Stools (four) were negative for parasites and one stool culture negative for the typhoid group. Blood (two) negative for malaria. Some of the blood pictures were as follows: September 28, 1924—R.B.C. 4,220,000; W. B.C. 10,450; Hem. 80%; S.M. 30%; Polys. 65%; Eosin 4%. October 13, 1924—R.B.C. 3,900,000; W.B.C. 6,300; Hem. 80%; Polys. 60%; Eosin 2%. October 28, 1924—R.B.C. 4,180,000; W.B.C. 8,150; Hem. 80%; Polys. 60%; Eosin 2%. November 28, 1924—W.B.C. 6,000; Polys. 45%; Eosin 5%. Blood culture negative for typhoid group. Blood culture (two) negative for B. Melitensis.

Melitensis agglutinations: October 15, 1924—Positive plus (1-640 dilution). October 16, 1924—Positive double plus. January 5, 1925—Positive plus (1-320 dilution). June 18, 1925—Positive plus.

Blood Wassermanns (three) were double plus early in the disease but later all Wassermanns and provocative Wassermanns were negative. Blood chemistry normal.

The treatment was entirely symptomatic except that:

1. Quinine was given by mouth for a period with no results.

2. Neoarsphenamine 0.3 gms. was given on one occasion with no results. (On the second day of the second rise of fever.)

3. Mercurochrome (15 cc. of a 1% solution) was given intravenously once during the height of an exacerbation with no result except a quite severe general reaction. (On the tenth day of the second rise of fever.)

Case II

E. H., white, female. Age thirty-two years. Admitted January 2, 1925. Family history: Unimportant. (This patient was the wife of a medical officer of the army who was a laboratory specialist and who had been doing considerable work with Malta fever for the previous few months. History revealed no other opportunity for infection with B. melitensis.) Previous personal history: Malaria at eleven years. Typhoid at sixteen years. Otherwise unimportant. Present illness: On December 6, 1924, had feeling of marked depression; that night a slight chill. For three days following had severe headache. From then until December 25th was up part of time and in bed part of time with headache, pain in back, chilliness, etc. Appetite very poor. Constipated. On December 25, 26, 27, and 28, had severe chill about 4:00 P. M. Had severe headache and some fever each time. Temperature persisted, going up to 102° F. plus. Cough developed and on afternoon of December 31st had slightly blood streaked sputum. None afterward. Had lost twelve pounds in past three months.

At time of admission complained of headache; slight, dry cough; marked weakness; heavy drenching sweats occasionally in afternoons; poor appetite; marked constipation.

Physical examination showed nothing of note other than a prolapsed uterus. Well nourished. Spleen not enlarged. Urine and stools negative.

Blood Counts: January 3, 1925—R.B.C. 4,350,000; W.B.C. 7,200; Hem. 80%; Polys. 67%. January 5, 1925—R.B.C. 4,100,000; W.B.C. 7,150; Polys. 70%.

January 3, 1925—Blood negative for malaria. January 7, 1925—Blood negative for malaria. Blood Wassermann negative.

Blood Cultures: January 2, 1925—Four specimens at two hour intervals were negative (no growth).

Blood Agglutinations: January 3, 1925—B. melitensis positive, double plus. January 6, 1925—B. melitensis positive, 1-1280 dilution. Typhoid, Para A and Para B negative. January 11, 1925—B. melitensis, positive 1-2500 dilution. January 4, 1925—Urine culture negative.

Fever continued for twenty-four days, with morning remission and afternoon rise up to 102.4° F. There was then a remission lasting for fourteen days and she was allowed to go home.

Symptoms during stay in hospital were the temperature, chilly sensations followed by sweating, marked physical and mental depression, fleeting joint pains in various joints, and constipation. The spleen was never palpated.

The symptoms of physical and mental depression and occasional slight elevations of temperature persisted for some months after leaving the hospital but there was no actual prolonged curve as seen in Case I.

Treatment was symptomatic.

Case III

W. M., white, male. Age twelve years. Admitted July 12, 1926. Family history: Mother died of carcinoma of cervix uteri. One brother has tuberculosis of right hip. Otherwise unimportant. Previous personal history: Scarlet fever in early childhood. Tonsillectomy in 1921. Triple typhoid inoculation (three injections) in 1921. About three and one-half weeks before admission patient had an attack of sore throat which lasted two or three days during which he had fever ranging from 100 to 104° F. After the attack of sore throat disappeared the fever persisted, within the variations above noted; otherwise he felt fairly well. No headache. Occasional pain in the abdomen. Bowels had been moving two or three times daily in past week.

Only complaints on admission were of occasional pain in abdomen, two or three fairly loose bowel movements daily for past week, temperature of from 100 to 104° F. for past three weeks.

Physical examination was negative except for slight gaseous distention of the abdomen. X-ray of chest negative. The urine negative. Stool culture negative for typhoid group. Blood count: R.B.C. 4,090,000; W.B.C. 6,150; Hem. 80%; Polys. 32%. July 12, 1926—Agglutination for typhoid fever 1-160. Paratyphoid A and B negative. Malta fever positive, 1-1200. July 13, 1926—Blood culture negative for typhoid group. July 15, 1926—Agglutination positive for B. melitensis 1-1000. July 22, 1926—Agglutination positive for B. melitensis, 1-1000.

The temperature persisted from 102.6° F., gradually declining by lysis to normal over a period of eight days; then two days remission and a slight rise of temperature again to 100° F., this exacerbation lasting three days. The original temperature curve thus lasted for about thirty-two days. The only symptom noted in hospital was slight headache. There were no gastrointestinal symptoms. The spleen was not palpated at any time. Convalescence was slow but uneventful. Treatment symptomatic.

Case IV

L. B. F., white, male, age seventeen years. Date of admission July 22, 1926. Family history: Unimportant. Previous personal history: Unimportant. History of present disease: Had been feeling badly for several days before admission to hospital, with some malaise. Was in infirmary at the military academy, where he was attending school, for several days before admission to hospital. At time of admission seemed dull mentally and complained of dizziness when in the erect position. Physical examination showed an occasional cardiac extra systole; a few sibilant râles in the lungs posteriorly; otherwise negative. Spleen not enlarged.

X-ray of chest negative. Urine showed a trace of albumin; otherwise negative. Stools negative for parasites.

Blood Counts: July 23, 1926—W.B.C. 4,750; Hem. 70%; Polys. 53%. July 24, 1926—W.B.C. 8,950; Hem. 80%; Polys. 70%. July 27, 1926—W.B.C. 6,200; Polys. 47%. July 28, 1926—W.B.C. 4,950; Polys. 64%. Blood negative for malaria on July

23, 1926 and July 24, 1926. On July 27, 1926 the blood agglutination for typhoid fever, 1-80. Para-typhoid A 1-80, Para-typhoid B 1-160. B. melitensis 1-1200. Blood culture negative. July 28, 1926—Stool culture negative for typhoid group. July 30, 1926—Blood agglutination, typhoid 1-80. Para-typhoid A 1-80. Para-typhoid B 1-160. B. melitensis 1-1200. July 31, 1926—Blood culture negative for typhoid group and for B. melitensis. August 17, 1926—Blood agglutination positive for B. melitensis 1-650.

The temperature on admission to the hospital was 100.1° F. The day following it was 104° F. and thereafter ranged from 105.2° F., gradually declining by lysis to normal over a period of twenty-seven days; it was then normal for twenty-four hours when it was again elevated to a maximum of 103.8° F., declining by lysis over a period of eight days. Following this there was a normal intermission for four days, followed by an elevation to 100° F., for two days, after which it continued normal. The pulse rate was proportionate to the temperature. Respirations within normal limits.

The only symptom other than the temperature was constipation. Treatment symptomatic throughout. Discharged from hospital on August 26, 1926, feeling perfectly well and had no symptoms thereafter.

Case V

C. H. W., white, male. Age twenty-one. Date of admission October 11, 1926. Family history: Unimportant. Previous personal history: Unimportant. History of present disease: For one week before admission to hospital he had noticed that he felt "weak and feverish" in the afternoons and had dull pain in the back and abdomen. The day previous to admission the weakness was marked; there was vertigo, and the pain in the back and abodmen was increased. Symptoms increased during the day, leading to his being sent to the hospital the following morning.

On admission he complained of slight cough; dull aching pain in abdomen and back; weakness and dizziness when in erect position.

Physical examination: Showed a slight generalized adenopathy and some tenderness to pressure over lower abdomen. X-ray of lungs negative. Of four specimens of urine examined one showed albumin. Stools negative.

Blood Counts: October 15, 1926—R.B.C. 4,670,000; W.B.C. 6,350; Hem. 80%; Polys. 66%. October 16, 1926—W.B.C. 5,200; Polys. 62%. October 18, 1926—W.B.C. 5,400; Polys. 64%. October 28, 1926—W.B.C. 4,800; Polys. 58%. November 6, 1926—W.B.C. 6,700; Polys. 58%. December 16, 1926—W.B.C. 7,250; Polys. 65%.

Blood negative for malaria. Blood Wassermann negative. Blood culture negative. Blood agglutination negative for typhoid group; positive for B. melitensis, 1-1200.

November 17, 1926—Blood agglutination positive for B. melitensis 1-600. December 15, 1926—Blood agglutination positive for B. melitensis, 1-320.

Four days after admission it was noted that the spleen was enlarged and tender. Patient was running a high temperature. No other symptoms except the enlarged and tender spleen and marked constipation. He was given tartar emetic, 1% solution, intravenously as follows: October 18, 1926—Three (3) cc. October 25, 1926—Four (4) cc. November 1, 1926—Five (5) cc. November 8, 1926—Six (6) cc. November 15, 1926—Seven (7) cc.

Treatment otherwise was entirely symptomatic. The temperature persisted, having declined by lysis, until November 10, 1926, a period of thirty days. Following this it remained normal and there were no further symptoms of any kind.

Although the fact of the patient having previously had the triple typhoid vaccine is mentioned in but one case, it should be stated that each had had one or more courses of this vaccine at varying periods prior to the present illness; this undoubtedly accounts for the 1-160 agglutinations for typhoid in Case III and the 1-80 typhoid, 1-80 para A and 1-160 para B agglutinations in Case IV. It is

believed that the typhoid group was eliminated as the etiological factor in both cases; certainly they did not appear clinically to be typhoid.

As further items of interest it may be noted that the spleen was enlarged in but one case; sweating was present in but one case; joint pains occurred in two cases; constipation was a definite factor in four cases. No joint pathology was noted, only the complaint of pain. In one case there was slight frequency of the bowels (2 to 3 daily stools) for a week before admission to hospital.

In all cases the white blood count was normal or showed some leucopenia and the polymorphonuclear count tended to be low. The onset was insidious in four of the cases.

Cases I and II had a suggestive history for B. melitensis infection and it is of interest that both had a rather typical clinical course with a long drawn out convalescence. The three other cases had histories which were not suggestive (although all were milk users), a shorter total period of febrile reaction, seemed less ill and convalesced quickly.

Might we assume that Cases I and II were B. melitensis infections and Cases III, IV, and V, B. abortus infections?

Editorials

LESIONS OF LATENT SYPHILIS

The following consists of abstracts from a paper read by the editor in opening a discussion in the Section of Venereal Diseases at the Annual Meeting of the British Medical Association, Manchester, July, 1929, and is here reprinted at the request of a number of members of the College.

Leptomeninges

Lesions of latent syphilis occur very frequently in the meninges, being present in the great majority of cases. They vary greatly in intensity, from small, localized opacities or thickenings to more patchy or even generalized thickenings of the arachnoid and pia. They are found most frequently over the parietal and frontal lobes, usually over the sulci, and not over the convolutions. In the active latent lesions these meningeal thickenings and opacities appear microscopically as localized areas of a mild productive process with slight infiltrations of monocytes, plasma cells, and lymphoid cells. There is a proliferation and increase of the reticulo-endothelial cells of the membranes, with eventually cells of fibroblastic type leading to fibrosis. Small perivascular collections of lymphocytes and plasma cells may occur throughout the meninges; the number and degree of these being in proportion to the severity of the process. In many cases there is only a slight productive reaction, leading slowly to thickening and hyaline change in the membranes. The sharply localized character of these mild lesions is very striking. Often they are seen in the gross with difficulty, by oblique light or upon floating the membrane. In the old case of latent syphilis the process may be for the greater part healed or inactive; the membranes show hyaline thickening, while cellular areas may be found only after prolonged search. Every transition stage of severity may occur, from slight fibrosis of the meninges to the active and clinically recognizable form of syphilitic meningitis.

Brain

Localized perivascular infiltrations occur within the brain tissue of the latent syphilitic. They are precisely similar to those found in paresis and cerebral syphilis, the difference being only in number and degree. They occur usually throughout the frontal and parietal lobes, and near the ventricles. They are usually few in number; in some brains only one or two such infiltrations may be found on extensive examination microscopically. Here again all transition stages in degree and number of these lesions occur, up to active brain syphilis and paresis. In many cases of syphilitic psychoses these latent lesions are found in very moderate numbers associated with a moderate atrophy and gliosis of the

brain tissue, involving particularly the frontal lobes. It may be said that every latent syphilitic has localized lesions identical with those of paresis, the only difference being in the number and intensity of these lesions. The meningeal lesions and those of the brain tissue do not always show a corresponding degree of involvement; as a rule the meningeal lesions are more numerous and more marked than the cerebral.

Spinal Cord

Similar lesions are found in the meninges of the cord and in the cord itself, but less frequently than in the brain.

Heart

In my experience the heart of every male latent syphilitic has shown latent lesions, varying from small and few microscopic areas of increased stroma nuclei and plasma cell and lymphocyte infiltrations up to more diffuse areas of interstitial myocarditis. In the majority of latent syphilitic females these cardiac lesions do not occur, or are very small. Nevertheless, in some women more severe forms of syphilitic myocarditis do occur. The part of the heart usually involved in these latent lesions is the septum, and the anterior and posterior walls of the left ventricle near the apex, rather than the walls of the right ventricle, although in some cases the right ventricle has shown more marked involvement than the left. The lesions are usually intermuscular, rather than perivascular. In the mildest degree they consist of an increase in the number of stroma nuclei, the latter being arranged in single or double file, occasionally with large aggregations of nuclei between the muscle. These aggregations represent perivascular infiltrations around the smallest coronary branches. The infiltrations present a variety of cell forms: plasma cells, lymphocytes, monocytes, and cells of fibroblastic type. Occasionally polynuclears are are present. The chief characteristic of these infiltrations is their diffuse or patchy character. They are not sharply demarcated, but trail off irregularly into the neighboring heart muscle. The papillary muscles are often involved. Very characteristic is an increase of nuclei beneath the endocardium, the cells lying in two to five rows, closely crowded together. They appear to be derivatives chiefly of the subendothelial reticuloendothelial cells. The stroma often appears markedly edematous, as in congenital cardiac syphilis, and very frequently it gives a mucoid reaction with mucin-staining dyes. The more active the process, the more marked is the edema. Fibrosis of the myocardium is the eventual result of this interstitial proliferation and infiltration. Between the active infiltrations the heart muscle fibers are well preserved, often hypertrophic. As the active cellular infiltration diminishes and fibrosis results, the heart muscle becomes atrophic, and often shows fatty degenerative infiltration. In many cases the fibrosis of the stroma takes place without much change in the muscle fibers. Ultimately, however, atrophy of the muscle results, and there is a patchy fibrosis of the myocardium containing atrophic fibers. This latter distinguishes infarct scars from the syphilitic fibrosis; the former being more sharply circumscribed and

devoid of muscle fibers in their central portions, at least. Spirochetes may be found, often after prolonged search, in the active infiltrations, and even in the scar tissue, when the latter is still fairly cellular. When the fibrosis becomes hyaline it is impossible to find them. Hence the advantage of the Warthin-Starry method of straining spirochetes in single sections, permitting control of the histologic lesions. With the exception of the aortic, the valves are rarely involved in latent syphilis. The aortic valves are affected chiefly through the vasa vasorum of the aorta, and a certain degree of sclerosis of the aortic valves is almost always present in the latent syphilitic in later years. Acute exacerbations of the latent lesions occur without known cause, and are characterized by a polymorphonuclear infiltration, in which spirochetes are present.

The heart of the latent syphilitic usually shows at necropsy dilatation of the left ventricle or of both ventricles. In the great majority of cases there is no valvular lesion, although the sequela of bacterial endocarditis may be coincident in some cases. In the younger individual latent syphilis of the heart probably predisposes to secondary bacterial endocarditis, as numerous cases showing this combination have been observed. In the older cases the majority show no secondary valvular involvement. The great majority of cases of latent syphilis come into the clinic of internal medicine as patients showing more or less vague myocardial insufficiency, with symptoms of dyspnea, palpitation, slight or marked cyanosis, and chronic passive congestion. They represent a definite cardiovascular complex. When questioned as to the occurrence of rheumatic symptoms they almost invariably give affirmative answers, and the common clinical diagnosis is therefore "rheumatic heart," even in the absence of all evidence of valvular lesion. A progressive course downhill of increasing cardiac dilatation and insufficiency follows, and the cause of death in the latent syphilitic is most frequently "cardiac or myocardial insufficiency." To what extent this cardiac failure is due to the myocardial lesion or to the associated aortic lesions is usually very difficult to determine. At necropsy the heart is dilated, the wall thin and atrophic, with a certain degree of subendocardial fatty degenerative infiltration. The endocardium is usually more or less thickened and opaque. Cross-section of the heart wall will show more or less marked irregular areas of fibrosis, particularly in the left ventricular wall towards the apex. A cardiac death is a very frequent form of death for the latent male syphilitic, and a large percentage of the deaths occurring in middle life from "myocardial degeneration" are due to this cause.

Aorta

Latent active lesions are found in the aorta of every male syphilitic and in the majority of female syphilitics, although usually they are much less marked in the women than in the men. The lesion is essentially a disease of the vasa vasorum, consisting in obliteration and thickening of the walls of the small nutrient arterioles of the aorta, with plasma cell and lymphocyte infiltrations along the course of these vessels. The term "mesaortitis" is a

misnomer, as syphilis of the aorta does not affect primarily the muscle coat of the vessel, but is primarily localized in the vasa vasorum. The infiltrations are always more marked in the adventitia around the larger vasa vasorum than in the media, decreasing in size towards the intima. As the result of the obliteration of the nutrient vessels there is a slow infarction of the intima and inner portion of the media, resulting in sclerosis and atrophy of the muscle and degeneration of the yellow elastic tissue. In the mildest cases small infiltrations are found only in the adventitia and around the para-aortic blood vessels. The gross pathological picture in the mild cases of aortic syphilis is that of an area of aortic sclerosis or atherosclerosis. In many cases it cannot be diagnosed as syphilitic in character from the gross appearances. Even in aortas that appear normal latent syphilitic lesions can be found in the adventitia around the vasa vasorum. The gross appearance of any aorta cannot be taken as a criterion for the absence of active syphilitic lesions in its wall; only the microscopic examination can decide as to the absence or presence of syphilis. It is in the severe forms of aortic syphilis that characteristic lesions of syphilis show grossly in the form of irregular fissures and depressions in the intima with the characteristic porcelain-blue appearance. In the great majority of cases, however, the changes produced in the aortic wall by syphilis are covered up by the associated secondary sclerosis of intima and inner portion of the media.

Syphilis of the aorta may exist in three forms: with aneurysm; with aortic insufficiency and in the form of perivascular lesions around the vasa vasorum in the absence of both aneurysm and aortic insufficiency. The third form is by far the most common, but is rarely recognized by the clinician.. It may be either symptomless, or present the clinical syndrome of an aortalgia, or even that of angina pectoris. In the cases associated with aortic insufficiency the valvular lesion is the result of an extension of the syphilitic disease of the vasa vasorum of the aorta to those of the valves. In the cases with aneurysm the weakening of the aortic wall is usually due to a localized development of miliary gummas along the vasa vasorum in their course through the media. As in the case of the heart, acute exacerbations of latent aortic lesions occur without known cause. They are also characterized by a polymorphonuclear infiltration, and frequently by localized necrosis in the media. Spirochetes are easily demonstrated in the aortic lesions by the improved starch-gelatin modification of the Warthin-Starry method. They occur in the perivascular lesions, but are particularly likely to be found in the polynuclear infiltrations. They are usually not found in large numbers, but in small groups, in the latent lesions. In the acute exacerbations they may be present in very large numbers, and extending into apparently normal aortic tissue, some distance from the area of infiltration.

Para-aortic Vessels.

A favorite site of predilection for the latent lesions of syphilis are the small blood vessels of the para-aortic tissues. Thickening of the arteriole

walls occurs, often leading to marked sclerosis or to obliteration of the vessel, while active plasma cell and lymphocyte infiltrations occur around the vessels, particularly around the veins. These lesions may be very slight; in some cases they are the only evidences found of a latent syphilitic infection. Usually, however, the process is continuous with that involving the vasa vasorum of the adventitia. In more severe cases the lymphocyte infiltrations are marked, forming irregular cords of cells following the course of the vessels. They extend along the retroperitoneal vessels, and into the root of the mesentery. Spirochetes are found in these infiltrations in very small numbers; it is usually more difficult to demonstrate them in these areas than in the infiltrations extending along the aortic vasa vasorum. Very rarely small miliary gummas may develop along the course of these small para-aortic vessels.

Liver.

In both sexes the liver is usually the seat of latent syphilitic lesions. They consist essentially in plasma cell and lymphocyte infiltrations of the periportal tissue, leading eventually to fibrosis and a certain degree of chronic hepatitis. All stages of severity exist, from the mildest to the most severe forms of cirrhosis (hepar lobatum). The frequency of occurrence of a mild grade of atrophic hepatitis in latent syphilitics is very high, as is also that of hepar lobatum. The latter condition, in my experience, is much more frequent in women than in men. The percentage of liver involvement in my material appears to be on the increase, particularly in the cases given a modern treatment with the arsenicals. In fifteen successive necropsies on latent syphilitics performed in my laboratory during the last year there was found a chronic diffuse hepatitis, varying in degree from an early mild form to that of an advanced severe atrophic cirrhosis. The relation of this condition to the treatment rather than to the syphilis remains to be determined. It is probable that the diffuse forms of hepatitis are due to something else than the syphilitic infection, as the syphilitic forms of hepatitis are usually irregular and localized, instead of being diffuse. In the average case the liver presents grossly the picture of brown atrophy and chronic passive congestion, with slight or marked irregularity of the surface. In some cases the small periportal infiltrations occur in livers that otherwise appear perfectly normal. The demonstration of spirochetes in the hepatic lesions is more difficult and unsatisfactory than in the case of any other organ. They are found usually only in the most active areas of infiltration, and then in small numbers. Throughout the newly formed connective tissue they are not present, or at least cannot be demonstrated.

Pancreas.

Lesions of latent syphilis are common in this organ, in the form of an interstitial pancreatitis not arising from the pancreatic ducts. In the great majority of cases the process is very mild. The interlobular stroma is increased, edematous, and infiltrated with small collections of plasma cells and lymphocytes. The intralobular stroma is increased, the vessel walls are thickened,

and the islands may become fibroid. This lesion may be associated with diabetes, and has been the most common form of pancreatic disease seen in our diabetic material. I believe, therefore, that syphilitic pancreatitis may be one cause of pancreatic insufficiency, although not the only cause. In the severe forms the organ is small, and much firmer than normal, except in cases in which there is marked edema of the interlobular stroma, in which cases the organ may be larger and softer. Syphilitic pancreatitis is frequently of congenital origin, and may cause pancreatic insufficiency early in life. We have seen two cases of diffuse pancreatic fibrosis in congenital syphilitics with enormous numbers of spirochetes present in all parts of the gland. In the older milder cases the spirochetes are more difficult of demonstration, because, as a rule, they are few in number, and sharply localized in the active plasma cell infiltrations. They occur singly or in small groups. In a case of very active diffuse interstitial myocarditis occurring in a young man of 24 the pancreas showed large areas of infiltration, associated with the occurrence of aggregations of plasma cells and lymphocytes large enough to be regarded as miliary gummas.

Adrenals.

In latent syphilis these organs show almost constantly active infiltrations of plasma cells and lymphocytes varying in size and number from a few small infiltrations scattered through cortex and medulla, up to diffuse infiltrations of marked degree, with interstitial fibrosis and parenchymatous atrophy, and thickening of the capsule. These lesions are more frequent and more severe in women than in men. While in the average case of latent syphilis these lesions are not severe enough to produce any clinical disturbances referable to the adrenals, yet they may be severe enough to cause marked atrophy and fibrosis of these organs, with a typical picture clinically of Addison's disease. I have seen several such cases, and in my opinion the cases reported in the literature as Addison's disease due to atrophy of the adrenals are probably all of them due to syphilis. There has been an increasing number of such cases reported. Further, I believe that milder degrees of adrenal syphilis may be recognized clinically as a distinct syndrome consisting of low blood pressure, asthenia, irregular patches of pigmentation not marked enough to be regarded as typical of Addison's disease, and accompanied by more or less constant pain in the lumbar region. As has been shown, these cases respond to antisyphilitic treatment, with cure or great improvement in the symptoms. These cases of adrenal syphilis showing a syndrome which might be characterized as sub-Addisonian are probably fairly common among latent syphilitics. Spirochetes are easily demonstrated in the cellular infiltrations, but are usually present in small numbers.

Testis.

The testis of every latent syphilitic shows sooner or later a patchy interstitial orchitis, with atrophy of the germinal epithelium and hyaline fibro-

sis of the basement membrane of the tubules. The process is usually slow and prolonged over a number of years, but is progressive in character, and ultimately the entire organ may become atrophic and hyaline. It preserves its normal size and consistency, however, in spite of the most marked change. An early loss of spermatogenic function occurs in the majority of those who have had syphilis. Owing to its patchy character and the involvement of individual lobules some sperm may continue to be produced by lobules which are not involved in the process. The interstitial cells usually appear hyperplastic and show a brown pigmentation. In spite of this hyperplasia there is generally a loss or reduction in sexual desire and potency on the part of the latent syphilitic. Spirochetes are found in the intertubular-cellular infiltrations that are present in the earlier course of the process. They have been found even in the lumen of the tubules and in the hyaline stroma of the basement membrane. They are numerous in the earlier stages, but are extremely difficult to demonstrate in the later atrophic stages.

Ovary.

I have never found a syphilitic lesion in the ovary, or, at least, any lesion that I could convince myself was due to syphilis. Spirochetes are common in this organ in congenital syphilis, but have never been found in it in acquired syphilis. This organ appears to be immune to the spirochetes; if not absolutely immune, it at least possesses a very high degre of relative immunity.

Tubes.

The same thing is true of the tubes. They appear to posses a high degree of immunity to the localization or action of the spirochete. I have never seen any lesions in the tubes of the latent syphilitic woman that I could feel convinced were syphilitic in nature; and I have never found any spirochetes in the tubes in acquired syphilis. As is true of the ovary, spirochetes are abundant in the tubes of the syphilitic newborn.

Uterus.

Syphilis of the uterus is by no means rare, both in the primary and in the later stages of the infection. In only a few cases in the latent syphilitic woman have I observed typical syphilitic lesions in the endometrium and extending into the uterine wall, along its smaller blood vessels. There were characteristic perivascular plasma cell and lymphocyte infiltrations, as found elsewhere in the body. Spirochetes were present in small numbers.

Lymph Nodes.

Latent syphilitic lesions are commonly present in the form of a chronic lymphadenitis which is essentially vascular or perivascular in character. It can usually be recognized histologicaly only when the process is marked. In such cases spirochetes are fairly abundant.

Lungs.

Consideration of this organ has been reserved to the last because of the uncertainty of diagnosis of pulmonary latent syphilis. It is true that the latent syphilitic presents a very high percentage of pulmonary fibrosis and chronic passive congestion (indura-

tion). Localized patches of fibrosis, usually regarded as chronic bronchopneumonia, are extremely common in thea lungs of latent syphilitics, but unless there is a gumma present in association, it is practically impossible to diagnose these fibroses as syphilitic in nature. The infiltrations are less perivascular and show fewer plasma cells than those in other organs, and the fibrosis predominates. The demonstration of the spirochete is the deciding criterion of pulmonary syphilis, and in the usual necropsy case of latent syphilis this is practically impossible. I have seen not more than fifteen cases in which the presence of pulmonary syphilis was positively proved. The majority of these cases were associated with gummatous lesions; in the others the process was essentially a disease of the pulmonary arteries (cases of Ayerza's disease). Spirochetes have been demonstrated in the vessel walls of such lungs.

Summary

It will be seen from the preceding descriptions that the lesion of latent syphilis repeats the essential pathology of the hard chancre and of the secondary and tertiary lesions of the active stage of syphilis, in that it is predominantly vascular and perivascular, and that the infiltrations are derived from the proliferation of cells *in situ*. Each localization of the spirochete leads to the production of what is essentially a miniature chancre. The presence of plasma cells and lymphocytes in the tissues in the form of localized perivascular infiltrations may be taken as the criterion for the presence of *Spirocheta pallida*. The organisms, therefore, persist in the tissues, producing slight lesions leading eventually to fibrosis and atrophy of the parenchyma. Clinical symptoms will arise only when this atrophy and fibrosis reaches such a degree that functional disturbance results. In the average case in the male this functional inadequacy appears first usually in the cardio-vascular system, and death from latent syphilis is most frequently due to cardiac insufficiency. There are, however, especial organ susceptibilities to the localization of the spirochete: in one individual the central nervous system, in another the liver, in a third the adrenals, etc., may bear the brunt of the latent infection, so that the clinical picture and the manner of death may vary greatly, according to the organ or tissue chiefly involved.

I have never seen at necropsy a case of perfectly healed syphilis. Search, often prolonged, always reveals active latent lesions in aorta, heart, or other organ. This is as true of cases treated in the modern manner as it is of cases treated with the old mercurial method. If any difference results in the two methods of treatment it would appear to be in the more frequent occurrence of chronic hepatitis in cases treated by the arsenical method. What the treatment accomplishes in either case is the more rapid reduction of the averace active case to a stage of latency. There is no evidence pathologically that the case of syphilis ever becomes wholly free from spirochetes. The latency of the infection may last throughout the individual's life; or at any time exacerbations may take place, and the disease arise above the clinical

horizon. What determines these renewals of virulence on the part of the spirochete, whether it be due to a changed quality on the part of the organism or to changes in the resistance of the body, we do not know. The possibility of such a clinical renewal of activity on the part of the spirochaete is always a possibility hanging over the head of the individual who once acquires this infection. Even if the disease never again produces a clinical outbreak, the relatively immune syphilitic will nevertheless develop various functional inadequacies as the price of the latency of his infection. These minute local infiltrations of plasma cells and lymphocytes represent the processes of a local tissue immunity. With time this immunity mechanism in itself becomes dangerous to the individual through the functional inadequacies which it may eventually produce. Whether a consistent five-year period of treatment would finally rid the body entirely of spirochaetes I cannot say, for in my material there have been no cases that have been under continuous treatment for that period of time. The fact remains, however, that in syphilitics accorded what has been regarded by the clinician as thoroughly satisfactory treatment, with complete clinical cure, latent lesions of syphilis still present themselves on microscopical examination of the necropsy material derived from such cases.

Abstracts

The Modifying Influence of Dichlorethyl Sulphide on the Induction of Tumors in Mice by Tar. By I. Berenblum (Jour. of Pathol. and Bacteriol., Vol. XXXII, 1929, p. 425).

Three groups of mice, 40 mice in each, were treated in the following manner. One group received applications of tar containing 0.1 per cent mustard gas, on a small area of skin at about the middle of the back (tar plus mustard gas series). The other two groups acted as controls, one receiving applications to tar alone (tar control series), and the other 0.1 per cent solution of mustard gas in acetone alone (mustard gas control series). The applications were repeated on an average once a week. Previous to each application, the hair of the part was cut as short as possible with curved scissors, thus obviating the use of a chemical epilator with its consequent irritation of the skin. After a few weeks the hair ceased to grow in most of all three groups. The experiment was continued until all the animals had died, i.e., for a period of 50 weeks. Five mice in the mustard gas controls survived for 56 weeks from the commencement of the experiment, but the treatment with mustard gas was not continued beyond the 50th week. A few mice which developed large malignant tumors, and which appeared to be suffering, were killed; otherwise the treatment was continued until each animal had died in turn. Sections of the tumors were examined microscopically, and only those showing involvement of muscle, or secondary deposits (one case only) were counted as malignant. The original purpose of subjecting skin to repeated applications of mustard gas and tar was to induce an increase in the blood supply of the skin by means of the mustard gas, and to see how this would influence the induction of tumors as the result of the tarring. It was realized from the beginning that hyperemia was not the only change induced by the mustard gas. But finding that the mustard gas itself was not able to induce tumors when applied repeatedly to the skin, and seeing that the hyperemia appeared to be such a prominent factor, it was thought, that if the results fell into line with those of other workers, who used different methods of inducing hyperemia, as section of the sympathetic, such results would then be of value. Repeated tarring in itself leads to a dilation of the cutaneous blood vessels in mice and rabbits, which ultimately developed tumors, but in guinea pigs and rats, which were found to be refractory animals (Itchikana and Baum). These authors concluded, therefore, that hyperemia must be a primary factor in the induction of tumors. Contradictory results have been obtained as to the effects of hyperemia produced by the removal of the cervical sympathetic ganglia and the induction of tumors by tarring. In the present experiments with the use of mustard gas, an almost complete inhibition of the induction of tumors was observed. The problem of a possible relation between hyperemia and the induction of tumors is therefore no nearer solution by the methods adopted in these investigations. However, the discovery of a substance, which is able to act on an animal so as to make the skin refractory to a carcinogenic tar, is not only of interest in itself, but may be used as an important tool in investigating many problems concerned with the processes underlying the experimental induction of warts. If mustard gas is able to inhibit the induction of warts by tar, the question arises whether this effect is something specific for mustard gas, or whether other irritants may not behave in a similar manner. The possibility of other such substances existing may necessitate a modification of the whole conception of the mixtures of chemical substances label-

led as "non-carcinogenic," because, if a trace of mustard gas, added to a carcinogenic tar, can so mask its carcinogenic effect, other substances capable of acting similarly may occur naturally in such "non-carcinogenic substances." In view of the above observations, one is no longer entitled to assume, if a tar or other mixture of chemical is found unable to produce tumors when painted on susceptible animals, that it contains no carcinogenic principles. One possibility certainly is that no such principle is present, but the other possibility is that, though present, it cannot produce tumors because some other substance is also there which causes the skin to become refractory, as is the case with mustard gas. The author concludes that the addition of 0.1 per cent mustard gas to a carcinogenic tar inhibits the tar from inducing tumors. This anti-carcinogenic effect of mustard gas is due to its action on the animal, so that the skin no longer responds to a carcinogenic tar. The induction of warts is still inhibited if the mustard gas is added to the tar as late as the 11th week of tarring.

Spectographic Examination of Pellagrin's Sera. By L. C. Scott, R. H. Turner, and H. S. Mayerson (Proc. of the Soc. f. Exper. Biol., October, 1929, p. 27).

That exposure to direct sunlight produces or intensifies the erythematous eruptions on the exposed parts of the bodies of pellagrins is an opinion of many observers; the underlying cause of this apparent photo-sensitization is, however, entirely obscure. The auto-experiment of Meyer-Betz with hematoporphyrin and the skin manifestations of hydroa aestivalis, buck wheat disease and other forms of apparent sensitization among the lower animals at least justify the suspicion that some toxic substance is circulating in the blood stream. With the object of determining whether or not the spectrum of pellagrous serum differed materially from that of non-pellagrous, a series of 13 sera was examined with a Hilger quartz spectograph. Each case had been admitted to the New Orleans Charity Hospital, and all were in the acute stage with characteristic eruption, usually with marked oral and gastro-intestinal symptoms. The sera obtained from these patients were examined for the absence or presence of hematoporphyrin, or for any possible differences in the spectrum of the pellagrous serum and that of normal serum. The instruments used were a large E 4 Hilger quartz spectograph and a quartz cell measuring ¾″ by ¼″ by ⅛″ internal diameter. An arc between two adjustable rods of soft Norwegian iron served as the source of radiation. This arc serves as efficient source not only for the visible but for the ultra-violet part of the spectrum as well. In no instance were the investigators able to detect sufficient difference btween the spectra of normal and pellagrous sera to warrant the conclusion that they were not spectroscopically identical. Furthermore, comparison between normal serum containing traces of hematoporphyrin and pellagrous serum left no room for doubt that this substance, at least in any detectable quantity, is not present in the circulating blood of pellagra victims. The examination of the urine from an acute case likewse showed no evidence of the presence of hematoporphyrin in the spectogram.

A Rapid Precipitation Test for Syphilis. By L. Rosenthal (Proc. of the Soc. f. Exper. Biol. and Med., October, 1929, p. 61).

This test unlike the other existing precipation tests for syphilis requires no dilution of the serum and antigen, either before or after mixing them. Therefore the tests deals with only two ingredients: serum and antigen. The serum is obtained and inactivated in the usual way. As only small amounts of serum are needed, it may be sufficient to secure the blood from the finger. The antigen is prepared by adding 2% solution of cholesterin in acetone to an equal volume of alcoholic beef heart extract, which is obtained by adding 5 cc. of 95% alcohol for every gram of beef heart muscle powder from which the ether soluble substances were previously removed by ether extraction. It is advisable to keep in stock separately the alcoholic extract and cholesterin solution, and to prepare mixtures sufficient for only one week's need. If cholesterin crystals precipitate out the solution is placed in an incu-

bator at 37° in order to dissolve them. If a turbidity occurs during the mixing of the cholesterin solution and the alcoholic extract, it is necessary to centrifugalize the mixture and use the supernatant clear fluid. In order to make the final results more conspicuous for reading 0.05 methylene blue powder is added to 10 cc. of the cholesterinized antigen. For every test there are needed: 1, A hollow ground slide; 2, two capillary pipettes, one for the serum and the other for the antigen. In order to have the same caliber of the capillary stem for serum and for antigen, both pipettes are drawn from the same piece of tubing. As a standard, pipettes are used which contain 8 drops to 0.1 cc. of serum. 3, A glass rod. The technique of the performance of the test is as follows: Four drops of serum are placed in the cavity of the hollow ground slide, and one drop of antigen is floated on the surface of the serum and allowed to stay for 2 minutes. Then the serum and antigen are mixed thoroughly with a glass rod, the slide is gently tilted and rocked for one half minute and then examined. If the room temperature is low it is recommended to use serum and antigen which have been warmed in the incubator at 37° for 15 minutes. It must be borne in mind that the ratio of 4 drops serum to 1 drop antigen in reality constitutes a volumetric ratio of about 8 to 1, inasmuch as the surface tension of the antigen is only one-half of that of the serum. The slide is examined under the low power microscope (magnification 1:80), the diaphragm being sufficiently narrowed. The reaction is clear cut. In negative sera the whole field is uniformly bluish and has a fine granular appearance without any clumping. This appearance becomes particularly evident when the lens is focused upon the surface layer. In positive sera a definitely marked clumping is observed. The clumps are stained more intensely than the surrounding fluid. Their size varies. Big clumps indicate a strongly positive reaction; clumps of medium size are reported as a positive reaction, and fine delicate clumping is reported as a dubious reaction (±). The clumping is very characteristic and can be easily distinguished from other particles which may be due to the impurities of the serum, to the incomplete dispersion of the antigen in the serum, or to the presence of precipitated cholesterin crystals. The test was performed on 1066 sera and checked by the Wassermann reaction. Of 739 that gave a negative Wassermann there were 735 that were negative and 4 positive by the Rosenthal test; of 228 giving a strongly positive Wassermann, 228 gave a positive Rosenthal; of 58 giving a positive Wassermann, 55 were positive by the Rosenthal test and 3 dubious; of 38 dubious by the Wassermann, the Rosenthal gave 19 positive, 17 dubious and 2 negative; of 3 anticomplementary by the Wassermann, the Rosenthal gave 2 negative and 1 positive. There is then an almost perfect agreement of the two tests. In weak positive and dubious Wassermann sera this test gives a more clear cut reaction. Thus, the test combines reliability with technical simplicity.

Experiences with the Gerson-Diet in Pulmonary Tuberculosis. By Erich Schwalm (Klin. Wochschr., October 15, 1929, p. 1941).

In the German daily press there have appeared statements that by means of the Gerson diet the severest cases of pulmonary tuberculosis have not only greatly improved but have been practically cured. On the other hand in the scientific tuberculosis literature there has been only unfavorable mention of the method and its results. Schwalm put 20 cases of pulmonary tuberculosis on the Gerson diet in connection with mineralogen and phosphorus cod-liver oil. In some of the cases the use of cod-liver oil was omitted in order to try out more conclusively the effects of the Gerson diet and the mineralogen. As a substitute for the phosphorus cod-liver oil recresal was given. In spite of the fact that there was no difficulty in making the diet palatable, yet in the majority of the patients there arose sooner or later a disinclination, or even a pronounced aversion to the salt free diet. Schwalm regards this as a point of some importance in relation to the use of such a diet for tuberculous patients who frequently suffer from loss of appetite. The mineralo-

gen was always unwillingly taken. From his experience with these 20 cases, the author draws the following conclusions. In no one of the twenty cases of pulmonary tuberculosis treated by the Gerson diet was any improvement of the pulmonary condition noted. In these patients no objective change could be observed, that could be interpreted in the sense of a detoxication or alteration in tone. The weight increase fell within the same limits as occurs ordinarily under Sanatorium treatment. For the increase in weight the phosphorus cod-liver oil appeared to be of the greatest moment, a fact already known in tuberculosis therapy. No advantage on the part of the Gerson diet could be shown over the usual diet of the German Sanatoria in which the vitamines also play a part. The author closes with the wise remark that in case of a more extensive trial of the Gerson diet, such should be placed in the hands of experienced tuberculosis therapeutists, who through their many years' experience in the management of large Sanatoria are fitted to make accurate observation and judgment of the results of such treatment.

Reviews

Diseases of the Stomach. A Textbook for Practitioners and Students. By Max Einhorn, M.D., Emeritus Professor of Medicine at the New York Post-Graduate Medical School and Hospital; Consulting Physician to the Lenox Hill Hospital, New York. Seventh Revised Edition. 593 pages, 131 figures. William Wood and Company, New York, 1929. Price in cloth, $6.00.

The first edition of this work appeared in 1896. That this is the seventh shows that it has been of service to the profession in its more than thirty years in which it has been available. During this period there has been great progress made in our knowledge of gastro-enterology. Particularly has Roentgenology contributed greatly toward a more refined and definite diagnosis in some of the organic diseases of the alimentary tract. The author thinks that the especial attention paid to the pathologic conditions of the tract has led to a disregard of neurotic and functional disorders, to the detriment of a host of sufferers. In the former editions a prominent place was given to these functional ailments, and in this new edition they are left in the same position of importance. While there is much of value contained in this book, its background and many of the statements made in it impress the reader as being out of date. For instance, the part which constitution plays in gastric disease is not considered; and the writer leans to the parasitic theory of cancer etiology. Roentgenology receives far too inadequate treatment.

Varicose Veins. With Special Reference to the Injection Treatment. By H. O. McPheeters, M.D., F.A.C.S., Director of the Varicose Vein and Ulcer Clinic, Minneapolis General Hospital; Attending Physician New Asbury and Fairview Hospitals; Associate Staff of Northwestern Hospital, Minneapolis, Minn. 208 pages, illustrated with half-tone and line engravings. F. A. Davis Company, Philadelphia, 1929. Price in cloth, $3.50.

This book is a resumé of a most thorough investigation of the world's literature on the subject of the injection treatment of varicose veins, combined with the care and treatment of approximately 800 cases actually treated at the Out Patient Department of the Minneapolis General Hospital. The author has been impressed with the amount of disability that accompanies the extreme and complicated cases of varicose veins, and by the fact that many such patients become invalids for life, when under proper care and treatment they might again be made useful members of society. He does not believe that the medical profession as a whole realizes the importance of this condition. The time honored and accepted excision of the offending vein, in the hope of cure, has been unsuccessful in such a large percentage of cases that we must seek new and more effective methods of treatment. The failure of surgical treatment of varices led the author to adopt the injection method. A thorough review of all the methods of injection that have been used is given, the technic is fully and clearly described, as are the complications and sequelae. It is a concise and clear statement of the most important facts concerning the injection method.

Clinical Medicine for Nurses. By Paul H. Ringer, A.B., M.D., Formerly Chief of Medical Service of the Asheville Mission Hospital; and on Staff of Biltmore Hospital, Biltmore, N. C. Third Revised Edition. 330 pages. Illustrated. F. A. Davis Company, Philadelphia, 1929. Price in cloth, $3.00.

The first edition appeared in 1918, the

second in 1924. After five years the third is necessary. Since the fundamentals of diagnosis and treatment have changed little in this time, and as conservatism is essential in a book of this kind, not many changes have been made in the material. As the book is one for nurses only, variant views are not emphasized; and as the work is intended solely as a background for teaching purposes, it has been considered wise to rid the book of dogmatic statements in order that the teacher may be able to set forth his own views. The object of these lectures is to place in concrete form a fairly detailed description of the points in the various diseases that nurses will be expected to observe and interpret; and also to form a basis upon which class-room lessons can be assigned and quizzes held, the teacher amplifying as he sees fit. Basteriology and pathology have been very sketchily traced. The main points dwelt upon have been symptoms and their meaning, complications and their detection, as far as the nurse is concerned. Physical signs have been almost wholly set aside. Treatment is dealt with in a general manner. The book is the first of its kind in the field. It appears to cover the ground intended very thoroughly, and will prove a very useful book for training schools. It may be recommended for this purpose.

The Female Sex Hormone. Part I. Biology, Pharmacology and Chemistry; Part II: Clinical Investigations Based on the Female Sex Hormone Blood Test. By Robert T. Frank, A.M., M.D., F.A.C.S., Gynecologist to Mount Sinai Hospital, New York. 321 pages, 86 illustrations and 36 graphs. Charles C. Thomas, Springfield, Illinois, and Baltimore, Maryland, 1929. Price in cloth, $5.50.

This monograph is based upon twenty-five years of laboratory and clinical research, and embodies and amplifies the material presented in the Charles Sumner Bacon Lectures, at the University of Illinois School of Medicine, 1928. It presents a review of our present knowledge concerning the female sex hormone, and assembles into a comprehensive whole the many fragmentary, yet more or less complementary, reports which have accumulated. The study of the female sex hormone, which is a growth substance, that has gradually become more and more specialized, until it has developed into the main factor causing "femininess" in all dimorphous species, has now reached the critical stage in which we may hope at any time to obtain it in pure substance. The sole object of this monograph, the author asserts, is the defense of no thesis, but is the presentation of our present state of knowledge as far as is warranted by the actual proved facts. Unquestionably, modifications in both hypothesis, as well as in theory, will be required. The book performs a distinct service as a compilation of knowledge in this especial field. The literature is quite fully given. It is nicely printed, and well illustrated.

Atlas of the History of Medicine. Anatomy. By Dr. J. G. DeLint, Lecturer on the History of Medicine at the University of Leyden. With Foreword by Charles Singer. 96 pages; illustrated with 199 Portraits, Views of Anatomical Theatres, Anatomical Drawings, Title-Pages of are Books. Paul B. Hoeber, Inc., New York, 1926. Folio, Cloth, $6.00 net.

This is a history of Anatomy presented in the form of portraits, reproductions of anatomical drawings, views of the interiors of anatomical theaters, reprints of the title-pages of rare books written by the masters of medicine in the past, arranged in chronological order, and giving the story of the rise and development of anatomical science. With each illustration there is printed a concise description, which assigns the subject its evolutionary position and dates it accurately in its historical sequence. For the understanding of a science it is necessary to understand the history of its development. This is perhaps more obviously true of anatomy than of any other science, for almost the first things a student learns in anatomy are the names of early anatomists. It is fortunate that in anatomy, as in no other science, the names of the great masters and thinkers, who have in their turn, helped to build up the great edifice of anatomical knowledge, should be so inseparably con-

nected with the various parts of the body originally described by them. Anatomical terminology is in itself a perpetual reminder of the scientific achievements of the past. Alas, that modern anatomists have attempted to supplant this picturesque old historical terminology by one that is devoid of any appeal to the imagination. It is necessary to bring medical history to the modern student of medicine in a form quickly and easily assimilable; and this can best be done, as DeLint has done it here, through the medium of illustrations, since most students have learned to take their impresions chiefly through the eye. This method also makes immediately available to the reader material that is inaccessible to the ordinary reader. The perusal of several hundred selected pictures arranged chronologically can give a very good idea of the progress of the knowledge they embody. No demand is made upon the reader's linguistic abilities, and the pictures will appeal to him in that medium through which he is most accustomed to receive impressions. The chief aim of this atlas is to give a picture of the evolution of anatomy from the earliest times to the present day. A classical picture of an anatomical procedure, the portrait of one of the great masters of anatomy, or the title page of one of the great anatomical treatisse of the past cannot help but fix the memory of some anatomical discovery. While the chief aim dí this work is to aid the study of anatomy, it is hoped that it may find a place in the library of the practitioner who is culturally interested in the history of medicine. It is an atlas that should be in possesion of every student of medicine in his freshman year, while engaged in the study of anatomy. Anatomy remains the foundation stone of medicine. It has a long and fascinating history; this atlas will convey to the student something of the truly romantic side of this most important branch of medical study.

The Medical Museum. Modern Developments, Organization and Technical Methods. Based on a New System of Visual Teaching. By S. H. Daukes, O.B.E., M.D., D.P.H., D.T.M.&H., Director of the Wellcome Museum of Medical Science. Affiliated to the Bureau of Scientific Research. An Amplification of a Thesis Read for the Degree of M.D., Cambridge. 172 pages, 44 illustrations. The Wellcome Foundation, Ltd., London, England, 1929.

The experience obtained in organizing and establishing the Wellcome Museum of Medical Science forms the basis upon which this volume has been developed. This experience has demonstrated the practicability and value of such a Museum, which treats of medicine as a whole, and is now regarded as a necessary adjunct to any well-equipped school of medicine. In it are stored, in a condition of preservation more or less effective for teaching purposes, specimens which offer unique material for education and research. Around this center, in the wards, out-patient department and autopsy rooms, revolves a wealth of material illustrating the classic or abnormal manifestations of disease. These manifestations do not necessarily lend themselves to display in a museum jar; indeed, such a jar is too often merely a testimony of failure. As the years pass, there develops an increasing number of ways of depicting the manifestations of a morbid process: the radiograph, electro-cardiograph, the kinematograph, the photograph and painting are all available for making such a complete record of disease. Since more and more instruments have been invented which enable the diagnostician to see into the hidden recesses of the human body: the laryngoscope and ophthalmoscope have been followed by the sigmoidoscope, the cystoscope and many other instruments, by which it has become posible to make exact pictures of conditions which can be rarely seen at the autopsy or in the collections of the Hospital Museum. As a whole the medical museums have not kept pace with these clinical and diagnostic advances, and it is good for us to survey the situation, and to see if, by further development on new lines, we may not provide something of real value for present and future generations. In such an effort has the system described in this volume been conceived, as a form of medical museum which will link up the various branches of medical work into one

demonstration, providing a display which may be fittingly termed *synoptical*. This system is now being developed in the Wellcome Medical Museum, which has been described as the most effective medical museum in the world, in its successful methods of illustrating in the most vivid and instructive way the present state of knowledge of the causation of human disease, and the methods of prevention and treatment. It is both museum and library combined: "it is in effect a sumptuously illustrated textbook. In chosen parts of the subject a student may learn more from a quiet hour in one of its divisions than he is likely to gain from any ordinary formal lecture of the schools." This volume outlines the development of the medical museum along synoptical lines, the need for reform and the evolution of the new system. Chapters on general arrangement and classification, etiology, pathology, symptomatology, treatment and prevention are given, with the technical methods employed in the elucidation of these subjects. In numerous appendices are given directions as to building, cases, labels, illustrations, mounting of specimens, methods of preservation, etc. This volume is very timely and should prove most useful to American Medical Schools, in which the synoptical sumeum is for the greater part unknown and unheard of. Only in McGill and Toronto, on this Continent, has the medical museum been made an active factor in the teaching of medicine. In the United States museum teaching remains almost wholly undeveloped or wholly lifeless.

The Respiratory Function of the Blood. Part II, Haemoglobin. By Joseph Barcroft, Fellow of King's College, Cambridge. 200 pages, 63 figures. University Press, Cambridge, 1928. Price in cloth 12/6.

The first volume of this series, "Lessons from High Altitudes" was published in 1925. Owing to the rapid advance of knowledge, Professor Barcroft found it impossible to revise his orignal volume on "The Respiratory Function of the Blood" for a second edition. He has, therefore, decided to break up the work into a series of manageable units, originally intended to correspond more or less to the "Parts" of the original work. The present volume deals with haemoglobin regarded as a chemical substance. It makes no profession of dealing with the red blood cell, or with the properties of blood. These will form the subject of another volume; so that the consideration of many now classical investigations, such as those of the Rockefeller Institute and the Monogram of Henderson, is reserved for the present. After an introductory chapter, the chapters of this book respectively with porphyrins, haemochromegen, cystochrome, specificity of haemoglobin, specific oxygen capacity, manufacture of haemoglobin, nature of haemoglobin solution, molecular weight of haemoglobin, dissociation curve of haemoglobin, theories of the union of oxygen with haemoglobin, kinetics of oxyhaemoglobin in dilute solutions, interaction of carbon monoxide with reduced haemoglobin, effect of temperature on haemoglobin and the biological significance of haemoglobin. For the specialist in the physiology of the blood and for the investigator this volume is indispensable, containing as it does all that is known of haemoglobin from the chemical side.

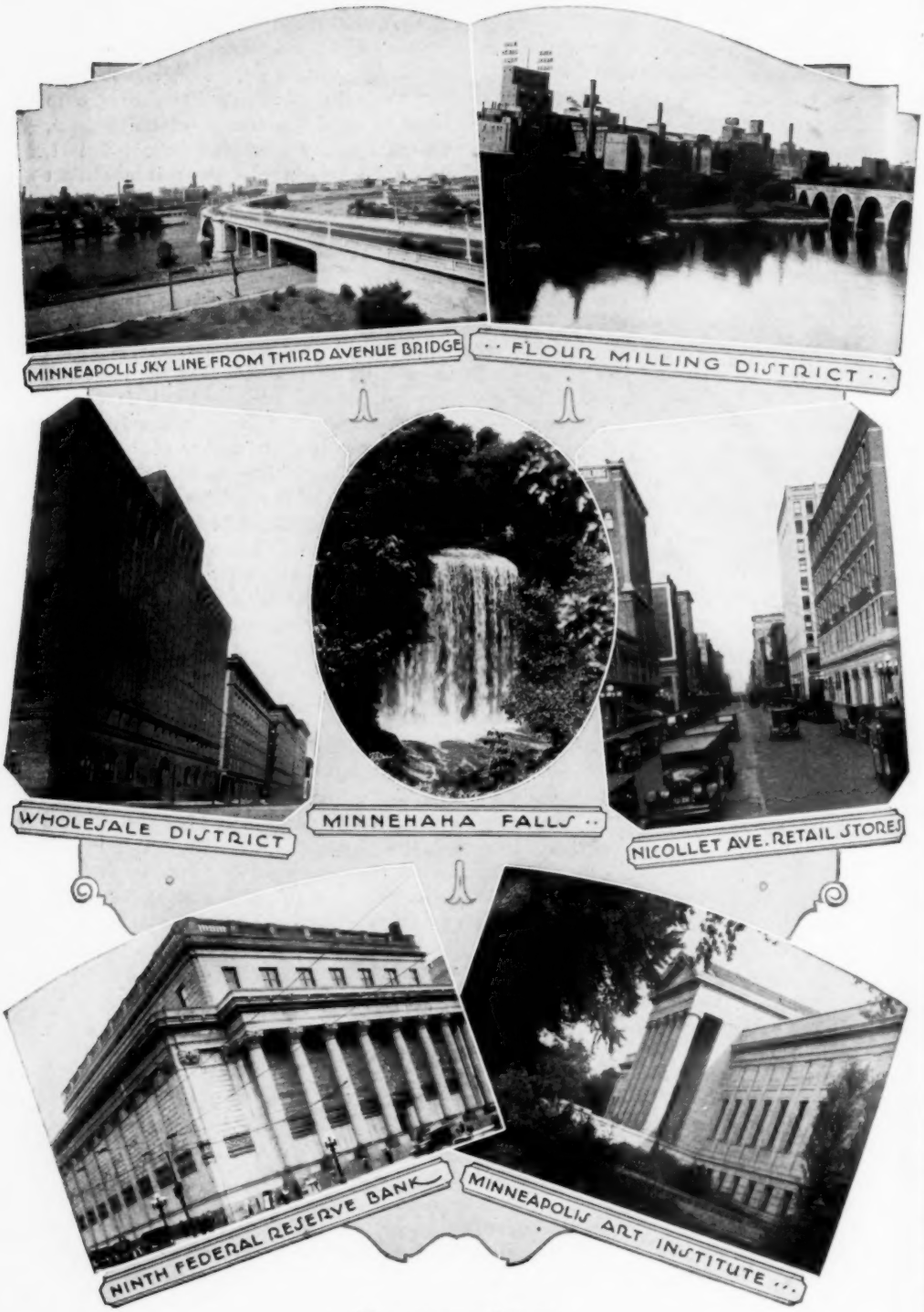
Health Behavior. A Manual of Graded Standards of Habits, Attitudes and Knowledge Conducive to Health of the Physical Organism, and of Personality, Home, Community and Race. By Thomas D. Wood, M.D., Professor of Health Education, Teachers College, Columbia University; and Marion Olive Lerrigo, Ph.D., Staff Associate, American Child Health Association. 150 pages. Public School Publishing Company, Bloomington, Illinois, 1927.

This manual has been in preparation by the authors for several years, and is in part an outgrowth of the scale of health habits set up in "Health Education" the report of the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association. That scale was originally set up by the authors of this Manual, and approved by the Joint Committee and the Technical Committee of Twenty-seven. That scale included only habits, not attitudes or knowledge, and

is only for the kindergarten and first three grades. In the present manual the scale of health habits, attitudes and knowledge has been extended to the High School period and early adult life. In a general way the criteria set up in this manual for the different age-period development are extremely good and satisfactory; and the book may well be recommended as a general guide for the intelligent parent in the education and development of the progeny. There is one danger, apparently not recognized by the authors, of too dogmatic and categorical statement regarding such things as diet. The indivdual peculiarities and idiosyncrasies of human individuals are apparently not considered at all in these scales. For instance, the statement is made that "each person should have one quart of milk daily, drinking a glass at each meal, and getting the rest in the preparation of foods." This is dangerous teaching, for what about the effect of such milk drinking upon a child or person who is sensitized to milk, and to whom milk is actually a poison, producing asthma, urticaria, and a host of severe disturbances. The reviewer is surprised that such an unwise general advocacy of a milk diet escaped the attention of the Joint Commitee. This is another example of the danger of too little knowledge on the part of people who set themselves up as able to form general health criteria applicable to all human individuals. Aside from this very serious criticism, the reviewer grants that there is much that is praiseworthy in the conception and practical application of this manual.

Studies in Nutrition. An Investigation of the Influence of Saltpeter on the Nutrition and Health of Man with Reference to Its Occurrence in Cured Meats. By Harry S. Grindley and Ward J. MacNeil. Vol. II, Discussion and Interpretation of the Data Relating to the Health and Physical Condition of the Men. With the Assistance of Josephine E. Kerr and William S. Chapin. From the Laboratory of Physiological Chemistry, Department of Animal Husbandry, University of Illinois, 1929.

The manuscript copies of the various chapters of this volume were completed in 1911. The delay in publication has been due to factors beyond the control of the authors. To the careful reader of Volume I and II, it will be evident that there is a distinct conflict between the two joint principal authors of this report. This conflict concerns personal viewpoint, methods of presentation and interpretation of scientific data, and apparently in some instances, even accuracy of record of observations. Perhaps the existence of such a conflict makes for a more reliable report of the investigation. However that may be, it is certain that the great delay in publication is related to it, inasmuch as the author of the present volume has ben without authority or responsibility in respect to administrative and financial arrangements. The various positive deductions presented in this volume have been recognized only after diligent search in a somewhat confusing mass of recorded data. The deductions and conclusions of each individual chapter standing as a unit are far less convincing than when those of all the various chapters are considered together. The results of the experiments on bacteria and enzymes support the indication of protective effect of saltpeter in relation to food poisonings, as well as its influence upon the intestinal flora. They also throw a flood of light upon the indication of irritant action of potassium nitrate upon the stomach, and offer a logical explanation of the gastrointestinal irritation, suggested by the blood examination and of renal irritation. In giving prominence to positive findings in a field so controversial, and of such practical importance to particular industries, it has been fully realized that definite and specific points have been presented for discussion, attack and refutation, and that such attacks may be expected. While it is sincerely hoped that any mistakes or false deductions in this work will be exposed and refuted, it it also hoped that such false deductions contained in it may be found to be unimportant.


MINNEAPOLIS SKY LINE FROM THIRD AVENUE BRIDGE
·· FLOUR MILLING DISTRICT ··
WHOLESALE DISTRICT
MINNEHAHA FALLS ··
NICOLLET AVE. RETAIL STORES
NINTH FEDERAL RESERVE BANK
MINNEAPOLIS ART INSTITUTE ···

Minneapolis Scenes

Where We Meet — February 10-14, 1930

Fourteenth Annual Clinical Session

College News Notes

The material for the scientific program for the Fourteenth Annual Clinical Session of the College is practically complete. The outline of the five days' program is as follows:

MONDAY, FEBRUARY 10

Morning:	Registration
Afternoon:	Opening Session, which will include the addresses of welcome and part of the scientific session
Evening:	Scientific Program

TUESDAY, FEBRUARY 11

Morning:	Clinics
Afternoon:	Scientific Session
Evening:	Scientific Session

WEDNESDAY, FEBRUARY 12

Morning:	Clinics
Afternoon:	Scientific Session
Evening:	Convocation, followed by Smoker

THURSDAY, FEBRUARY 13

Morning:	Clinics
Afternoon:	Scientific Session, short, followed by General Business Meeting at 4:00 o'clock
Evening:	Banquet

FRIDAY, FEBRUARY 14

Morning:	Clinics
Afternoon:	Scientific Session

The program for the morning sessions in the laboratories and clinics of Minneapolis contains a wealth of material, the outline of which will appear in the final printed program, to be sent to each member of the College. There are, besides the clinics in the University Hospital, the demonstrations in the various laboratories at the University, the clinics in the laboratories and lecture rooms of the Minneapolis General Hospital and of the other hospitals taking part in the clinical program, evidence of a large amount of work of current interest that will be attractive to every member of the College.

In addition to these, one or two items are worthy of especial interest. The first of these are the demonstrations to be given at the Agricultural College of the University. The group of chemists, biologists and nutritional experts on the Agricultural Campus is preparing some demonstrations which would seem at first to the outside the realm of interest of the practicing physician, but the local committee has been astonished and greatly pleased to learn of the many subjects to be presented and the extraordinary interest these

clinics and demonstrations will have for the physician and the scientist. The workers on the Agricultural Campus are manifesting an enthusiastic response to our invitation and will give work of a character which the members of the College will do well to study.

At Glen Lake Sanatorium the Superintendent and staff, together with a large and active consulting staff, are preparing a program of unusual attractiveness and interest. This institution is the Hennepin County Sanatorium for tuberculosis, with over 700 beds, and the spirit of investigation and study is one worthy of attention on the part of the members of the College and their guests. The interest of the staff is not limited to the custodial care of the tuberculous, but includes all the medical problems arising in so large a group of individuals.

In addition to the outline of the program which is attached, papers have been promised by Dr. Allen K. Krause of the Desert Sanatorium, Tucson, Arizona, Dr. Charles A. Elliott of Chicago and Dr. William Gerry Morgan of Washington, D. C. Inasmuch as their formal titles are not as yet at hand, the definite place of each in the daily program is not yet assigned, but the mention of these names is sufficient to call attention to the interest their presentations will have.

The program as outlined is tentative and may be subject to some minor changes.

MONDAY, FEBRUARY 10, 1930

OPENING SESSION, 2:30 O'CLOCK

THE AUDITORIUM

1. Addresses of Welcome.
   Lotus Delta Coffman, President of University of Minnesota.
   Elias P. Lyon, Dean of University of Minnesota Medical School.
   Edward L. Tuohy, Duluth, Minnesota, President of the Minnesota Society of Internal Medicine.
   J. T. Christison, St. Paul, Minnesota, President of the Minnesota State Medical Association.
   E. L. Gardner, Minneapolis, President of the Hennepin County Medical Society.
2. Reply to Addresses of Welcome.
   John H. Musser, Jr., New Orleans, President of the American College of Physicians.
3. Colloids in Medicine.
   Ross A. Gortner, Minneapolis.
4. Cerebral Localization.
   Lewis J. Pollock, Chicago.
5. The Physiological Panel in Diagnosis and Prognosis.
   Walter Freeman, Washington, D. C.
6. Gastro-Intestinal Troubles that Now Go Undiagnosed.
   Walter C. Alvarez, Rochester, Minn.

EVENING SESSION, 8:00 O'CLOCK

THE AUDITORIUM

1. Latent Hyperthyroidism Masked as Heart Disease.
   Samuel A. Levine, Boston.
2. Observations on the Etiology of Gall-Stones.
   A. C. Ivy, Chicago.
3. The Significance of Atelectasis in Bronchopulmonary Conditions.
   Frederick T. Lord, Boston.
4. Moving Pictures of the Results of Stramonium Treatment in Encephalitis.
   Frederick Epplen, Seattle.

TUESDAY, FEBRUARY 11, 1930

AFTERNOON, 2:00 O'CLOCK

THE AUDITORIUM

VASCULAR DISEASE

1. The Effect of Generalized Arteriosclerosis upon the Heart and the Systemic Circulation.
   George Fahr, Minneapolis.
2. Some Newer Aspects in the Problem of Essential Hyptertension.
   Norman M. Keith and James W. Kernohan, Rochester, Minn.
3. The Retinal Vascular Changes in Hypertension.
   Henry P. Wagner, Rochester, Minn.
4. Arteriosclerosis in Diabetes.
   Elliott P. Joslin, Boston.
5. The Relations of Arterial Sclerosis and Renal Disease.
   Alfred Stengel, Philadelphia.
6. The Causes of Arterial Hyptertension.
   E. T. Bell, Minneapolis.
7. The Management of Hypertension.
   James S. McLester, Birmingham.
8. The Use of Nuclear Extractives in Experimental and in Human Anemias.
   Noble Wylie Jones, Olaf Larsell and B. I. Phillips, Portland, Oregon.
9. The New Possibilities in Classification and Treatment of Anemia.
   Hilding Berglund, Minneapolis.
10. Cinematomicrographic Demonstration of Human Intestinal Protozoa. Pictures and Remarks on their Biology, Pathology and Treatment.
    John V. Barrow, Los Angeles.

TUESDAY EVENING, 8:00 O'CLOCK

THE AUDITORIUM

1. History of Syphilis.
   Joseph L. Miller, Chicago.
2. History of Certain Medical Instruments of Precision.
   Logan Clendening, St. Louis.
3. Spontaneous Pneumothorax, Non-tuberculous.
   F. J. Hirschboeck, Duluth, Minn.
4. The Healing of Tuberculosis, Illustrated by Films and Slides.
   Francis M. Pottenger, Monrovia, Calif.

WEDNESDAY, FEBRUARY 12, 1930

AFTERNOON, 2:00 O'CLOCK

THE AUDITORIUM

1. Splenic Puncture as a Diagnostic Procedure in Infancy and Childhood.
   Julius H. Hess, Chicago.
2. Indications and Technic of Sympathetic Ganglionectomy and Ramisectomy.
   A. W. Adson, Rochester, Minn.
3. Results of Sympathectomy in Peripheral Vascular Disease and Scleroderma.
   George E. Brown, Rochester, Minn.
4. Sympathectomy in Polyarthritis.
   Leonard G. Rowntree, Rochester, Minn.
5. The Relation of Experimental Rheumatoid Inflammation to Allergy.
   Benjamin J. Clawson, Minneapolis.

6. Rectal Temperature Curves; Normal and Abnormal.
   William B. Breed, Boston.
7. The Limitations of Heliotherapy in Pulmonary Tuberculosis.
   Bernard L. Wyatt, Tucson, Ariz.
8. Resumé of Our Present Attitude Regarding Iodine in the Treatment of Toxic Goitre.
   James H. Means, Boston.
9. Unusual Addison's Syndromes.
   A. B. Brower, Dayton, Ohio.
10. A New Method for the Treatment of Pellagra.
    Clyde Brooks, University, Alabama.
11. Hyperinsulinism and Dysinsulinism.
    Seale Harris, Birmingham, Alabama.
12. In Defense of the Stethoscope.
    James B. Herrick, Chicago.

THURSDAY, FEBRUARY 13, 1930
AFTERNOON, 2:00 O'CLOCK
THE AUDITORIUM

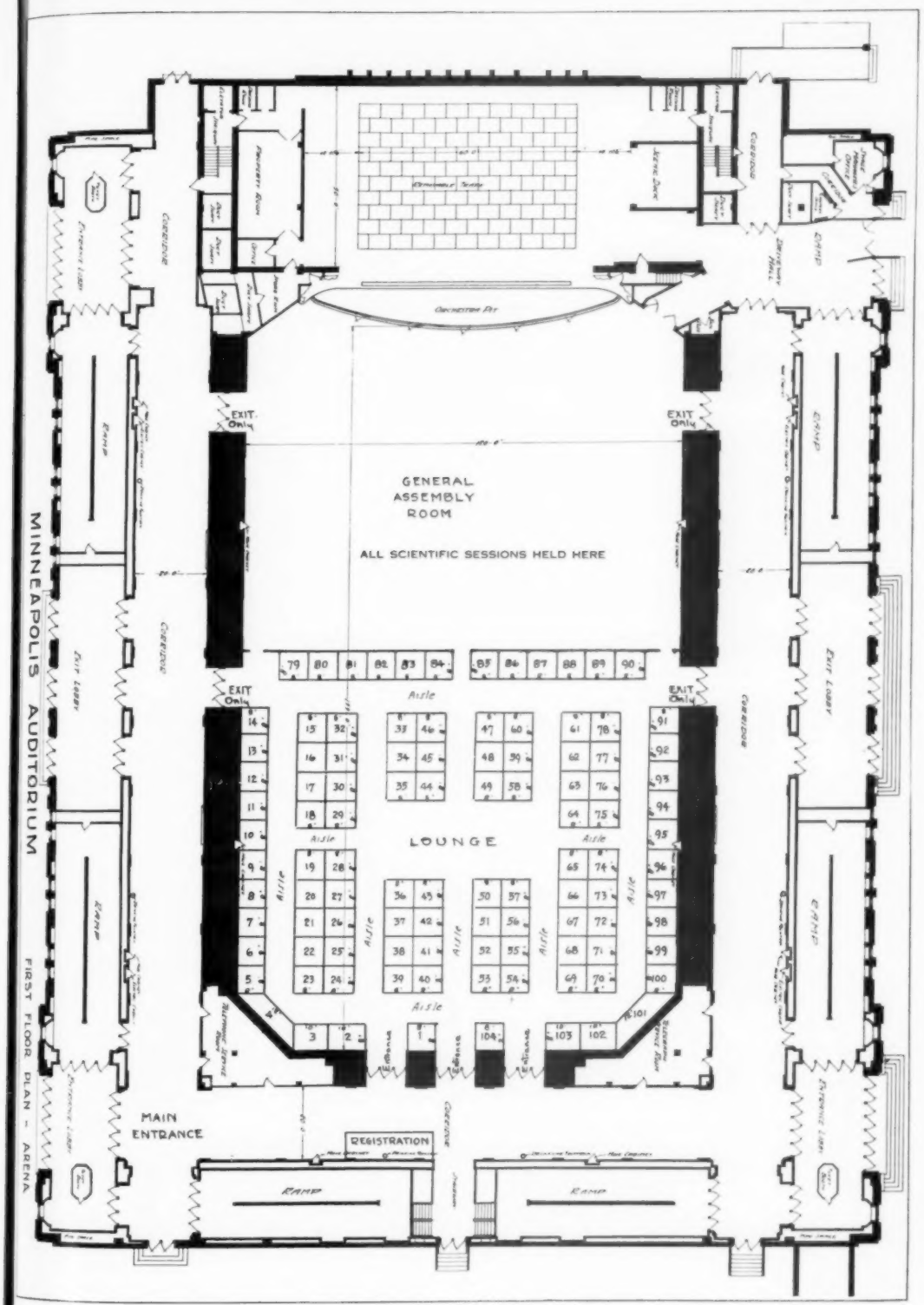
1. Symposium on The Biology of Cancer
   The Biology of Cancer, from the Experimental Standpoint.
   Leo Loeb, St. Louis.
   The Nature of Heredity in Animals.
   H. Gideon Wells, Chicago.
   Heredity of Cancer in Man.
   Aldred Scott Warthin, Ann Arbor.
   The Principles of Radiation Treatment.
   Francis Carter Wood, New York.
2. Undulant Fever in California.
   J. Edward Harbinson, Woodland, Calif.
3. Undulant Fever; A Clinicopathological Study.
   Walter M. Simpson, Dayton, Ohio.
4. Multiple Polyposis of the Colon.
   J. A. Bargen, Rochester, Minn.

The General Business Meeting of The College will be held at 4:00 o'clock in the Auditorium. All Masters and Fellows should attend.

FRIDAY, FEBRUARY 14, 1930
AFTERNOON, 2:00 O'CLOCK
THE AUDITORIUM

1. Symposium on The Rôle of Surgery in Pulmonary Tuberculosis.
   Pneumothorax.
   James Burns Amberson, Loomis, N. Y.
   Pneumolysis.
   Ralph C. Matson, Portland, Oregon.
   Multiple Intercostal Neurectomy and Phrenicectomy.
   John Alexander, Ann Arbor.
   Thoracoplasty.
   Philip King Brown, San Francisco.
   General Considerations of the Rôle of Surgery in Tuberculosis.
   Gerald Webb, Colorado Springs.
2. Rare Forms of Myelosis.
   Hal Downey, Minneapolis.

MINNEAPOLIS AUDITORIUM
FIRST FLOOR PLAN - ARENA



PLAN OF MINNEAPOLIS AUDITORIUM

showing layout of meeting hall, exhibits, registration, etc. The Exhibit and Exposition of medical appliances and apparatus, books, pharmaceutical products, special foods, etc. will be a special feature of the Clinical Session, February 10-14, 1930.

EXCERPTS FROM MINUTES OF THE MEETING OF THE BOARD OF REGENTS

AMERICAN COLLEGE OF PHYSICIANS

OCTOBER 27, 1929

The meeting of the Board of Regents was called to order at the College Headquarters in Philadelphia at 9:45 A. M., Sunday, October 27, 1929, by President John H. Musser, of New Orleans. Those present were: Drs. David Preswick Barr, George E. Brown, Arthur R. Elliott, Charles G. Jennings, Jonathan C. Meakins, James Alex. Miller, Sydney R. Miller, George Morris Piersol, Maurice C. Pincoffs, F. M. Pottenger, Alfred Stengel, Aldred Scott Warthin, S. Marx White, President Musser and the Executive Secretary, Mr. E. R. Loveland.

After the reading of the Minutes of the previous meeting, President Musser addressed the Board briefly, reporting, "The organization seems to me to be in excellent condition in every way, from the point of view of the type of members coming into the organization and from the point of view also of the excellency of the programs of the last few years and of the program to be put on next year. I think a great deal of the credit of this belongs to the two preceding Presidents and to the Regents for their whole-hearted coöperation—also the Governors."

The Executive Secretary reported the following deaths:

Fellows

Frank C. Balderrey	Tucson, Ariz.	May 9, 1929
Edgar O. Crossman	Washington, D. C.	June 21, 1929
Daniel Elliott	Newark, N. J.	.....
Rudolphus Wm. Gelbach	Hoboken, N. J.	August 2, 1929
Arthur S. Loevenhart	Madison, Wis.	April 19, 1929
C. W. McElfresh	Baltimore, Md.	.....
Charles S. McVicar	Rochester, Minn.	June 29, 1929
John Phillips	Cleveland, Ohio	May 15, 1929
Joseph Wm. Rowntree	Waterloo, Iowa	April 3, 1929
C. E. de M. Sajous	Philadelphia, Pa.	April 27, 1929
John A. Witherspoon	Nashville, Tenn.	April 28, 1929

Associates

Frank B. Granger	Boston, Mass.	October, 1928
James W. Cokenower	Des Moines, Iowa	April 16, 1929

The following resignations were presented and unanimously accepted on individual resolutions:

Fellows

James H. Dempster	Detroit, Mich.
John E. Heatley	Oklahoma City, Okla.

Associates

F. J. Eichenlaub	Washington, D. C.
Vincent Fenerty	Philadelphia, Pa.
George L. Pearson	Youngstown, Ohio

The following gifts to the College Library of publications by members were reported:

By Dr. George M. Albee (Fellow), Worcester, Mass., June 30, 1929
Reprint, "The Care of the Heart in Pneumonia."

By Dr. Alexander Bate (Associate), Louisville, Ky., Sept. 25, 1929
Reprint, "The Romance of George Rogers Clark and Therese de Leyba."

By Dr. Miles J. Breuer (Fellow), Lincoln, Nebr., May 9, 1929
Reprints, "Case Reports Illustrating Diagnostic Principles in Sexual Psychopathology"; August 5, 1929, "A Neglected Focus in Infection," "Suggestions for Effectiveness in Diagnosis."

By Dr. Grafton Tyler Brown (Fellow), Washington, D. C., Oct. 23, 1929
Reprint, "Cottonseed and Kapok Sensitization."

By Dr. Ralph O. Clock (Fellow), Pearl River, N. Y., May 17, 1929
Reprint, "The Treatment of Burns with Normal Horse Serum."

By Dr. C. J. Gentzkow (Fellow), Fort Sam Houston, Texas, June 19, 1929
Reprint, "Insect Pests in Texas."

By Dr. Edwin Henes, Jr. (Fellow), Milwaukee, Wis., May 1, 1929
Book, "Atlanta Proceedings of the Inter-State Postgraduate Medical Association of North America."

By Dr. Dale M. King (Fellow), Detroit, Mich., July 5, 1929
Book, "Why We Are What We Are."

By Dr. Philip B. Maltz (Fellow), Washington, D. C., June 11, 1929
Reprint, "Statistical Studies Bearing on Problems in the Classification of Heart Diseases."

By Dr. Aaron E. Parsonnet (Fellow), Newark, N. J., June 19, 1929
Reprints, "Physicians' Record System Conducive to Greater Efficiency"; "Insulin Treatment of Diabetes Mellitus; Report of Two Cases of Leukemia."

By Dr. Lewis M. Silver (Fellow), New York, N. Y., June 12, 1929
Reprint, "The Vanderbilt Clinic—A Retrospect."

By Dr. W. Blair Stewart (Fellow), Atlantic City, N. J., Sept. 28, 1929
Book, "A Synopsis of the Practice of Medicine."

By Dr. Carl V. Vischer (Fellow), Germantown, Philadelphia, Pa., Sept. 16, 1929
Reprint, "Chronic Ulcerative Colitis—Perforation and Peritonitis—Case Repart."

Dr. Guy L. Connor of Detroit, Michigan, by resolution, was reinstated as a Fellow of the College.

The following resolution was regularly adopted:

Resolved, That the Committee on Constitution and By-Laws shall thoroughly investigate and review the whole situation concerned with those members who were elected to Fellowship some years ago when the initiation fee or annual dues were $25.00 and $5.00 respectively, or less, and who subsequently were dropped from the College roll due to the non-payment of higher dues later prescribed.

Communications concerning various College activities were read from Dr. Walter M. Simpson, Dayton, Ohio, Dr. Miles J. Breuer, Lincoln, Nebraska, and Dr. Eben C. Hill, Baltimore, Maryland.

The Executive Secretary reviewed several communications from Fellows of the College concerning the advisability of maintaining a Placement Service through the columns of ANNALS OF INTERNAL MEDICINE and the Executive Offices. On resolution regularly adopted, the Executive Secretary was instructed to work out with the Editor of ANNALS OF INTERNAL MEDICINE, a suitable plan of printing announcements concerning positions to be listed through the Placement Service.

A letter from Dr. Arthur Bullard concerning the progress of the Committee on the Cost of Medical Care was read and briefly discussed. Dr. White suggested the possibility of having Dr. Ray Lyman Wilbur, Secretary of the Interior, to speak before the Fourteenth Annual Clinical Session, possibly on some subject having to do with medical economics, which would indicate the interest of the College in this subject, since Dr. Wilbur is the Chairman of the above mentioned Committee.

A resolution was regularly adopted authorizing Dr. Wilburt C. Davidson, Dean of the Duke University School of Medicine, to have the seal of the American College of Physicians carved on the new Duke Hospital.

After receiving the report of the Committee on Credentials through Dr. George Morris Piersol, Chairman, the following physicians were elected to Fellowship:

ELECTED TO FELLOWSHIP

OCTOBER 27, 1929

Arizona
Russell J. Callander, Tucson

Arkansas
Henry T. Smith, McGehee

California
Andrew Bonthius, Pasadena
J. Edward Harbinson, Woodland

Colorado
James H. Brown, Colorado Springs
Harry B. McCorkle, Colorado Springs

Delaware
Olin Sudler Allen, Wilmington

District of Columbia
Roger M. Choisser, Washington
Nelson Gapen, Washington

Florida
F. Clifton Moor, Tallahassee

Illinois
Charles A. Elliott, Chicago
Howard M. Jamieson, Decatur
Arthur E. Mahle, Chicago
Laurence H. Mayers, Chicago
Joseph L. Miller, Chicago
Warren F. Pearce, Quincy
Sidney A. Portis, Chicago
Italo Frederick Volini, Chicago

Indiana
Harold S. Hatch, Indianapolis

Kansas
Foster L. Dennis, Dodge City

Kentucky
Sydney E. Johnson, Louisville

Louisiana
Harold G. F. Edwards, Shreveport

Maine
Mortimore Warren, Portland

Massachusetts
Francis G. Brigham, Boston
Peter A. Colberg, Worcester
Maurice Fremont-Smith, Boston
William Mason, Fall River
Hugo A. Peterson, Worcester
Lester D. Riggs (U. S. V. B.), Rutland Heights
Howard Root, Brookline
Oliver H. Stansfield, Worcester
Henry S. Wagner, Pocasset

Michigan
Charles L. Brown, Ann Arbor
Trevor G. Browne, Battle Creek
Robert A. C. Wollenberg, Detroit

Minnesota
Mandred W. Comfort, Rochester
Edwin L. Gardner, Minneapolis
DeForest R. Hastings, Minneapolis
Peter Milton Mattil, Oak Terrace
Lillian L. Nye, St. Paul

Missouri
Joseph F. Bredeck, St. Louis
A. Morris Ginsberg, Kansas City

Nebraska
George W. Covey, Lincoln
Harrison A. Wigton, Omaha

New Jersey
Harold S. Davidson, Atlantic City
George H. Lathrope, Newark
James J. McGuire, Trenton
Carlos A. Pons, Asbury Park

New York
Louis Leon Klostermyer, Warsaw
Shailer Upton Lawton, New York
Earl C. Waterbury, Newburgh

North Carolina
James B. Bullitt, Chapel Hill
Sylvester D. Craig, Winston-Salem
Lewis W. Elias, Asheville
Philip W. Flagge, High Point
Thurman D. Kitchin, Wake Forest
Charles C. Orr, Asheville
Paul Henry Ringer, Asheville
James B. Sidbury, Wilmington

Ohio
Eugen G. Reinartz (M. C., U. S. A.), Dayton

Oklahoma
Henry T. Ballantine, Muskogee
Tom Lowry, Oklahoma City

Oregon
A. H. Ross, Eugene

Pennsylvania
William Devitt, Allenwood
George H. Hess, Uniontown
Eliah Kaplan, New Castle

Rhode Island
William P. Buffum, Providence

South Dakota
John L. Calene, Aberdeen

Texas
James E. Robinson, Temple
Samuel E. Thompson, Kerrville
John G. Young, Dallas

Utah
Ralph M. Tandowsky, Salt Lake City

Virginia
James W. Hunter, Jr., Norfolk
Garnett Nelson, Richmond

West Virginia
Oscar B. Biern, Huntington
Milton C. Borman, Montgomery
Adrian H. Grigg, Beckley
Frank C. Hodges, Huntington

Wisconsin
Karl E. Kassowitz, Milwaukee

Haiti
Kent C. Melhorn, Port au Prince

Hawaii
Harry L. Arnold, Honolulu

China
William W. Cadbury, Canton

After thorough discussion, the following resolution was adopted:

Resolved, that the Committee on Constitution and By-Laws be requested to enlarge upon the directions dealing with autopsy reports, making the directions more explicit and complete, this Committee to report at a later meeting of the Regents.

Dr. White, General Chairman of the Fourteenth Annual Clinical Session, at Minneapolis, February 10-14, 1930, gave a detailed report of arrangements for this Session. He suggested that a Friday evening meeting be eliminated due to the train service in Minneapolis. He presented each member of the Board with an outlined program of speakers and topics. He recommended, for the approval of the Board, having the Convocation on Wednesday evening and the Smoker following it.

The Executive Secretary reported upon arrangements for the Minneapolis Clinical Session made through his office. They included: reservations for Officers, Regents and Governors at the Curtis Hotel (the Curtis Hotel, though not specified as a headquarters hotel, will be the official hotel for the Boards of the College); reduced railroad fares throughout the United States and Canada on the Certificate Plan of fare and half fare; completion of arrangements for the Commercial Exhibit, consisting of one hundred and four booths with a gross rental amounting to $11,640.00; other miscellaneous arrangements for the smoother conduct of the business affairs of the College during the Session.

The following recommendation of the Committee on Clinical Session Guests was regularly adopted, after thorough discussion:

Resolved, That guests to the Minneapolis Clinical Session shall be admitted according to the following plan:

(a) Local guests, who are members of the Hennepin and Ramsay County Medical Societies, shall be admitted without any fee; furthermore, they shall be given the opportunity to subscribe to ANNALS OF INTERNAL MEDICINE at the rate of $5.00 per annum for the first year (the period during which the proceedings of the Minneapolis Session will be printed).

(b) Other visiting guests shall pay a registration fee of $15.00, and shall be entitled to one year's subscription to ANNALS OF INTERNAL MEDICINE, included within

the above fee; any visiting guest who does not desire the Journal, shall pay $12.00 registration fee.

Committee

S. Marx White, Chairman
James H. Means
John H. Musser
Sydney R. Miller

A resolution was regularly adopted requesting Dr. George E. Brown of the Mayo Clinic to prepare a suitable notice for printing in the Clinical Session Program concerning the receiving of guests at the Mayo Clinic during the February Session. Due to the fact that so many of the staff members of the Mayo Clinic will be in attendance at the Minneapolis Clinical Session, it will not be convenient for the Clinic to entertain visitors during that week. Visitors, however, will be welcome at the Mayo Clinic during the days preceding and following the Clinical Session.

Dr. Warthin, Editor of Annals of Internal Medicine, reported that everything is going very well. The subscription list has increased 50% and the arrangements are very successful. The Journal is being printed long in advance of the date of issue, and is distributed on time.

The following report, comparing volume, circulation and financial data of Volumes I and II of Annals of Internal Medicine, was presented in mimeographed form by the Executive Secretary to each member of the Board of Regents. He pointed out that Volume II had increased over Volume I by three hundred and sixty-six pages, and that the circulation of Volume II had increased over Volume I somewhat in excess of five hundred. The increased cose of Volume II over Volume I has been due to an increase in the budget for the Editor's office and an increase in the printing cost of the Journal due to its enlarged size. On the other hand, the income has been considerably increased through additional advertising and increased circulation. Although the report shows a small deficit, this will probably be considerably reduced by additional sales of Volume II. Furthermore, the Executive Secretary pointed out that the circulation of Volume III, now in process of publication, has been further increased (October 1929 issue, 2236), and that the volume of advertising is constantly growing, with the result that no further deficits are anticipated.

ANNALS OF INTERNAL MEDICINE

Cost of Annals

		Scientific Matter	Number of Pages News Notes Covers, etc.	Paid Advertising	Total
Volume II—July, 1928 to June, 1929		1195	254½	98½	1548
Volume I—July, 1927 to June, 1928		1008	163¼	10¾	1182
Excess pages, Vol. II over Vol. I		187	91¼	87¾	366*
Circulation, June 30, 1929	2018	Will be increased by future sales.**			
Circulation, July 1, 1927	1489	Increased by subsequent sales to date, 1782.			
	529	Increased circulation.			

Expenditures:						
Salaries			$ 2,693.33			$ 3,709.88
Equipment, Net						11.10
Postage & Telephone			568.12			684.09
Office Supplies			15.33			104.61
Printing		$ 9,065.54*			$11,365.28*	
Less Repayment for excess illustrations	$481.39			$261.42		
Less Inventory of stock	497.35	978.74	8,086.80	457.10	718.52	10.646.76
Traveling Expenses						42.50
Miscellaneous: (Editor's Office Copyright, etc.)			104.35			127.78
Net Cost			$11,467.93			$15,326.72
Income:						
Subscriptions; segregated from dues at $6 per member		$ 8,604.00			$10,038.00	
Direct Subscriptions		1,441.60			2,168.48	
Gross Receipts		$10,045.60			$12,206.48	
Less Expenses		46.00	$ 9,999.60		37.17	$12,169.31
Advertising:						
Gross Receipts		$ 204.22			$ 2,019.93	
Less Expenses		87.09	117.13		239.59	1,780.34
Net Income			$10,116.73			$13,949.65
Deficit			$ 1,351.20			$1,377.07**

*Printing costs increased due to 366 addition pages (30%) in Volume II.

**Deficit on Volume II will be considerably reduced through future orders.
Circulation of Volume III, October number, 2236.

The Executive Secretary submitted a report of the work accomplished during the summer months in the Executive Offices, especially the publication of the 1929-30 Directory of the College.

The following resolution, looking toward an improvement upon the working out of the present proposal system, was adopted:

Resolved, That the method of handling proposals of new members shall be changed to the following plan: The proposer after filling out the proposal form, signing the blank as proposer and securing the signature of a seconder, shall forward the proposal complete, along with personal letters, to the Governor, Regent or Officer who is acting as endorser, and that said endorser shall forward the entire proposal to the Executive Secretary with his own recommendations. There shall be a postal form that the proposer shall mail directly to the Executive Secretary notifying him of the fact that the proposal has been sent to the Governor, Regent or Officer for endorsement. This card to enable the Executive Secretary to follow up any proposals that do not come through promptly.

The Treasurer's report was submitted as follows:

"The Executive Secretary and the Treasurer have not deemed it necessary to make any detailed financial report at this time, since the Annual Audit and Complete Report will be made on December 31, 1929. The Finances of the College are in favorable condition. To September 30, 1929, cash receipts since January 1, totaled $66,725.91; cash disbursements, $55,871.11; balance, $10,854.80.

Since the last Regents' Meeting at Boston, it has seemed wise to invest some of our surplus in good securities. Accordingly, the Treasurer purchased on June 14, 10,000.00 par City of Philadelphia 4½'s at 102¼, or $10,225.00. On July 24, due to the maturity on August 1 of our 5,000 par Dominion of Canada 5½% bonds, the Treasurer sold same at par, $5,000.00, and re-invested in 5,000 par, Canadian National Railway 5's at 99¾, or $4,987.50, the balance on the sale being credited to our bank account.

(Signed) CLEMENT R. JONES, Treasurer."

This was the first meeting of the Board of Regents since the death of Dr. John Phillips in the Cleveland Clinic disaster, last May. Dr. Phillips had been a member of the Board of Regents and a member of the Executive Committee of the College for several years. The Treasurer reported that, on behalf of the College, an appropriate floral tribute had been sent to the Phillips home preceding Dr. Phillips funeral. The Secretary General reported that an appropriate obituary card had been sent to Mrs. Phillips.

After some discussion of ways and means, the following resolution was adopted:

Resolved, That the College shall grant a sum of money each year to be known as the John Phillips Memorial Fund and to be awarded for some outstanding piece of work in the United States or Canada; *Resolved,* further, that a Committee be appointed to formulate plans in detail and to recommend the amount of the Fund.

President Musser appointed the following committee to carry out the provisions of the above resolution:

DR. GEORGE E. BROWN, Chairman
DR. ALFRED STENGEL
DR. ARTHUR R. ELLIOTT

Due to the vacancy caused on the Board of Regents by Dr. Phillips' death, and in accordance with the provisions of the By-Laws, the following resolution was adopted providing for his successor:

Resolved, That Dr. James B. Herrick, Chicago, shall be and herewith is appointed a member of the Board of Regents, filling the vacancy caused by the death of Dr. John Phillips, until the next regular election at the Minneapolis Session.

The following Committee was appointed by the President to serve until the Board of Governors has elected successors thereto:

COMMITTEE ON CREDENTIALS FOR ASSOCIATION

Edgerton L. Crispin, Los Angeles, Calif. (Chairman)
Charles H. Cocke, Asheville, N. C.
Allen A. Jones, Buffalo, N. Y.
D. Sclater Lewis, Montreal, Quebec

The Board of Regents authorized a meeting of the Committees on Credentials early in January, in order that all proposals may be examined and recommendations prepared in advance of the Minneapolis Clinical Session. In accordance with the provisions of the By-Laws, no proposals will be acted upon preceding the Minneapolis Clinical Sessions unless filed before January 10, 1930. The Committee on Credentials, however, strongly recommends that all proposals be filed before the end of December, 1929.

E. R. LOVELAND, Executive Secretary.

Dr. John F. W. Meagher (Fellow), Brooklyn, is author of a book, "Masturbation and the Psychosexual Life," recently published by William Wood and Company.

The American Gastro-enterological Association has as its officers many members of the American College of Physicians: Dr. Frank Smithies (Master), Chicago, is President; Dr. Clement R. Jones (Fellow), Pittsburgh, is Second Vice President; Dr. Charles G. Lucas (Fellow), Louisville, is Secretary; Dr. Thomas Wray Grayson (Fellow), Pittsburgh, is Treasurer; Dr. George Morris Piersol (Fellow), Philadelphia, Dr. Franklin W. White (Fellow), Boston and Dr. Walter C. Alvarez (Fellow), Rochester, are members of the Council; Dr. Harlow Brooks (Fellow), New York, Dr. Allen A. Jones (Fellow), Buffalo, and Dr. Louis M. Gompertz (Associate), New Haven, constitute the Commitee on Admissions and Ethics.

Dr. Hugh S. Cumming (Fellow), Surgeon Geenral of the U. S. Public Health Service, Washington, D. C., is one of the incorporators of the National Institute of Psychology. The active members are made up of about fifty experimental psychologists, and their avowed purpose is to conduct a national laboratory for psychologic research "similar in some of its functions to the Bureau of Standards, but not under federal control."

Dr. Everett G. Geer (Fellow), St. Paul, addressed the Minneapolis Academy of Medicine, October 9, at the Town and Country Culb on "Evulsion of the Phrenic Nerve for Pulmonary Tuberculosis."

Dr. George H. Whipple (Fellow), Professor of Pathology and Dean of the University of Rochester School of Medicine, assisted in the conduct of a symposium on anemia before the Section on Medicine of the New York Academy on Medicine on October 15.

Dr. Vernon C. Rowland (Fellow), Cleveland, addressed the Academy of Medicine of Cleveland, October 18, on "Present Status of the Periodic Health Examination.

Dr. E. Roland Snader, Jr., (Fellow), Philadelphia, is author of an article, "A Modern Conception of Treatment of Cardiovascular Syphilis," which appeared in the September Issue of the Hahnemannian Monthly.

Dr. Lewellys F. Barker (Fellow), Baltimore, conducted two Clinics on October 31 and November 7 under the auspices of the Division of Medical Extension of the University of Maryland. Invitations and cards of admission were issued to various physicians of Maryland and surrounding territory by the President of the University and the medical faculty.

Dr. D. N. Silverman (Fellow), New Orleans, Associate Professor of Gastro-enterology in the Graduate School of Medicine of The Tulane University of Louisiana, addressed the South Texas District Medical Society at Houston, Texas, October 11, 1929, on "Chronic Ulcerative Colitis."

Dr. Sydney R. Miller (Fellow and President-Elect of the American College of Physicians), Baltimore, addressed the American Academy of Periodontology in Washington, D. C., October 10, on "The Value of Blood Chemistry in Periodontology." On October 18, he attended the meeting of the East Tennessee Medical Society, speaking on "The Maltreated Malnourished, Nervous Patient." As Councillor from the State of Maryland, he will attend the meeting of the Southern Medical Association in Miami in November, presenting before the Medical Section in Collaboration with Dr. Charles A. Waters (Fellow), Baltimore, a paper on "The Clinical and Roentgenological Value of Intravenous Cholecystography," illustrated by moving pictures.

Dr. E. J. G. Beardsley (Fellow), Philadelphia, addressed the Cumberland Valley Medical Association at Carlisle, Pa., on September 26, 1929. The subject was "The Common Psycho-neuroses of Every Day Practice."

Dr. E. Roland Snader, Jr. (Fellow), Philadelphia, is Vice President of the Eastern Homeopathic Medical Association, which held its Eighth Annual Convention at Wilmington, Delaware, on October 23, 24, 25 and 26.

The following Fellows of the College were represented on the program of the Eighth Annual Convention of the Eastern Homeopathic Medical Association at Wilmington, Delaware, on October 23, 24, 25 and 26 by the following papers:

Dr. G. Harlan Wells, Philadelphia, "Relative Efficiency and Stability of the Various Preparations of Digitalis."

Dr. Donald R. Ferguson, Philadelphia, "Problems in Diabetes."

Dr. G. Morris Golden, Philadelphia, "Auscultatory Percussion—its Value as a Diagnostic Measure."

Dr. E. Roland Snader, Jr., Philadelphia, "The Cardio-vascular Phenomena of the Menopause."

Dr. Joseph McFarland (Fellow), Philadelphia, addressed the Pathological Society of Philadelphia on October 10, his subject being "The New Bureau for the Study of Tumors."

Dr. William L. Rich (Fellow), Salt Lake City, and Dr. Maurice M. Critchlow (Fellow), Salt Lake City, were elected President-Elect and Secretary, respectively, of the Utah State Medical Association at the last annual meeting during July.

Dr. Howard R. Hartman (Fellow), Rochester, Minnesota, was one of the principal speakers at a graduate course arranged by the Utah State Medical Association at the Salt Lake General Hospital during September.

Dr. Wilburt C. Davidson (Fellow), Dean of Duke University School of Medicine, Durham, N. C., extended greetings to the University of Virginia Medical School at the dedication of its new $1,400,000 group of medical buildings, on October 22, during the annual meeting of the Virginia State Medical Society.

Dr. John Dudley Dunham (Fellow), of Columbus, Ohio, has been appointed consultant in Internal Medicine to the Student Medical Service of Ohio State University.

Dr. Crawford R. Green (Fellow), Troy, N. Y., addressed the Rensselaer County Medical Society, Troy, N. Y., Nov. 12 on "The Symptoms and Signs of Pneumonia."

Dr. David Riesman (Fellow), Philadelphia, Pa., will address the Atlantic County Medical Society, Atlantic City, N. J., on November 22, 1929. His subject will be "Diagnosis and Treatment of Nephritis and Nephrosis."

Dr. Harold S. Davidson (Fellow), Atlantic City, N. J., has been elected Vice President of the Atlantic County (N. J.) Medical Society.

Dr. Thomas F. Reilly (Fellow) of New York delivered a lecture to the Academy of Medicine of Newark, N. J., Thursday night, November 21, 1929, on "Headache."

Dr. Andrew Conrad Ivy (Fellow) gave an address on "The Newer Physiology of the Gall-Bladder," at the meeting of the International Postgraduate Assembly, in Detroit, October 25th.

At the same meeting of the International Postgraduate Assembly in Detroit, October 25, 1929, papers were read by Harlow Brooks (Fellow), New York, and Aldred Scott Warthin (Master), Ann Arbor.

On November 27, Dr. Aldred Scott Warthin (Master), addressed the Buffalo Academy of Medicine on "The Lesions of Latent Syphiils." Previous to the meeting, a large dinner was given Dr. Warthin, by Dr. C. W. Greene (Fellow) of Buffalo, at the Saturn Club.

George C. Hale (Fellow), Dean and Professor of Medicine, University of Western Ontario, London, Ontario, gave a diagnostic clinic on "Cardiovascular-renal Problems," at the Highland Park General Hospital, December 5, 1929.

Dr. Charles Jennings (Fellow), of Detroit, gave an address on "Pneumonia" before the St. Clair County Medical Society, on November 21, at Port Huron, Michigan.

Dr. Paul Roth (Fellow), of Battle Creek, Michigan, is the author of a paper on "Physiotherapy," in the December number of the Journal of the Michigan State Medical Society, for December, 1929.

Dr. W. H. Marshall (Fellow), of Flint, Michigan, has a paper on "Medicinal Therapeutics" in the Journal of the Michigan State Medical Society, for December, 1929.

Dr. Charles E. Stewart (Fellow), of Battle Creek, Michigan, has a paper on "Practical Dietetics in the Light of Modern Scientific Research," in the Journal of the Michigan State Medical Society, for December, 1929.